

Therapeutics

Effect of botulinum toxin type A on quality of life measures in patients with excessive axillary sweating: a randomized controlled trial

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Summary

Background Botulinum toxin type A (BTX-A) has been shown to be a safe and effective treatment for primary focal hyperhidrosis. However, the effect of BTX-A therapy on quality of life (QOL) in patients with this condition has only recently begun to be studied in controlled clinical trials.

Objectives To assess the impact on QOL of BTX-A treatment in patients with bilateral primary axillary hyperhidrosis.

Methods A multicentre, randomized, double-blind, placebo-controlled trial enrolled 320 patients who exhibited persistent, bilateral, primary axillary hyperhidrosis sufficient to interfere with daily activities. These patients were treated with either 50 U BTX-A (Botox®, Allergan, Inc., Irvine, CA, U.S.A.) or placebo in each axilla. QOL was assessed using the Hyperhidrosis Impact Questionnaire® (HHIQ) at baseline and 1, 4, 8, 12 and 16 weeks post-treatment, as well as the Medical Outcomes Trust Short Form-12 Health Survey® (SF-12) at baseline and 16 weeks post-treatment.

Results At baseline, participants reported a marked negative impact of hyperhidrosis on various measures, including emotional status, ability to participate in daily and social activities, productivity at work and number of clothing changes per day. During the post-treatment period, statistically and clinically significantly greater improvements in all of these parameters were observed for the BTX-A group compared with the placebo group ($P < 0.01$). The BTX-A group improvements were observed within 1 week of treatment, and were sustained with little or no decline throughout the 16-week follow-up period. Compared with the baseline HHIQ responses regarding treatment history, BTX-A treatment resulted in a greater level of overall treatment satisfaction than did many other hyperhidrosis treatments. In addition, patients treated with BTX-A exhibited statistically significantly greater improvement in the physical component summary score of the SF-12 at 16 weeks than did placebo-treated patients ($P \leq 0.019$).

Conclusions Hyperhidrosis is associated with a substantial QOL burden; however, QOL is markedly improved with BTX-A treatment.

Key words: axillary hyperhidrosis, botulinum toxin type A, endoscopic transthoracic sympathectomy, iontophoresis, quality of life, randomized controlled trial

Hyperhidrosis is an idiopathic disorder of excessive sweating commonly affecting body parts including the underarms (axillary hyperhidrosis), palms of the hands

(palmar hyperhidrosis), the soles of the feet (plantar hyperhidrosis), and the face (facial hyperhidrosis). This condition, which can be chronic, causes considerable disruption to both professional and social life, leading to severe deterioration in the patient's quality of life (QOL). This has recently been documented in a small

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number of patients using the Illness Intrusiveness Rating Scale.¹ Amir *et al.*,² using a hyperhidrosis-specific instrument, also demonstrated a negative QOL impact associated with hyperhidrosis. Among patients awaiting surgery for hyperhidrosis, they documented significant QOL impairments in functional, social, personal and emotional domains.

There is evidence that successful treatment of hyperhidrosis can lead to improvements in QOL. Patients treated with endoscopic transthoracic sympathectomy (ETS) for upper limb hyperhidrosis exhibit improvements in the mental and social domains of the Short Form-36[®] health assessment questionnaire³ and the Illness Intrusiveness Rating Scale.¹ However, when ETS is used to treat axillary hyperhidrosis, approximately 20% of patients are dissatisfied with the outcome,^{4,5} probably due in part to postoperative compensatory sweating, which has been characterized as major or disabling in approximately 26% of patients, based on clinical studies where the level of severity was assessed.⁶ Other surgical procedures include subcutaneous curettage⁷ and a modified liposuction technique, which is performed while the patient receives tumescent local anaesthesia.^{8,9} According to the limited data available so far, most patients experience reduction of sweating, and important complications, as in sympathectomy, can be avoided. However, exact evaluation of outcome, duration and satisfaction in large numbers of patients is lacking.

Satisfaction is limited with the majority of less invasive treatments for focal hyperhidrosis. Topical application of aluminium salts is effective only for a limited time (approximately 48 h) and the application is inconvenient and may cause skin irritation. Iontophoresis has been shown to be effective for palmar hyperhidrosis, with a reduction in sweating lasting for 3–4 days, but is unsuitable for axillary hyperhidrosis. Adverse effects of this technique are discomfort and skin irritation, including erythema and vesicles.¹⁰ Oral anticholinergic drugs used to treat hyperhidrosis are associated with poorly tolerated systemic side-effects, such as dry mouth and blurred vision, that limit their use.¹¹

Recently, local injections of botulinum toxin type A (BTX-A) have been shown to be a safe and effective treatment for chronic hyperhidrosis.^{12–14} BTX-A is a powerful inhibitor of acetylcholine release at the neuromuscular junction and at autonomic cholinergic nerve terminals. Small amounts injected into or near a cholinergic target tissue (e.g. muscle, sweat glands) cause a localized, long-lasting, but ultimately reversible

decrease in cholinergic transmission. This property of BTX-A has led to its widespread use in the treatment of a variety of disorders characterized by undesirable focal muscle overactivity and it is considered the treatment of choice for most focal dystonias.^{15–17}

The objective of the present study was to assess the QOL of patients with hyperhidrosis before and after treatment with BTX-A or placebo in a homogeneous population (primary axillary focal hyperhidrosis) using a hyperhidrosis-specific questionnaire, the Hyperhidrosis Impact Questionnaire[®] (HHIQ), and the Medical Outcomes Trust Short Form-12 Health Survey[®] (SF-12). Both safety and efficacy were found to be excellent; a full presentation of those results has been published elsewhere.¹³

Patients and methods

The present QOL assessment was conducted in conjunction with a large, randomized, double-blind, placebo-controlled comparison of the efficacy and safety of BTX-A in the treatment of axillary hyperhidrosis. Adult patients with persistent, bilateral primary axillary hyperhidrosis sufficient to interfere with the activities of daily life were enrolled from 17 European dermatology centres. This study complied with the Declaration of Helsinki and was approved by a local Institutional Review Board at each study site prior to study initiation. All subjects provided written informed consent. Patient inclusion criteria and treatment administration details have been previously described.¹³

Study protocol

Subjects were randomized in a 3 : 1 ratio using a block size of four to either the BTX-A (Botox[®], Allergan, Inc., Irvine, CA, U.S.A.) 50 U (to each axilla) treatment group or the placebo vehicle treatment group. The randomization schedule was produced with programming using the SAS[®] System for Windows, Release 6.12 (SAS Institute, Inc., Cary, NC, U.S.A.) and unique numbers were allocated to each subject and site. All medication vials were identical in appearance and were identified only by patient number.

Outcome measures

The HHIQ, a valid and reliable hyperhidrosis-specific questionnaire, was completed by patients at all

scheduled study visits. The questionnaire consists of two related modules: a 41-item module for baseline disease impact assessment and a 10-item module for follow-up longitudinal assessment and comparison with baseline. Copies of the HHIQ survey are available upon request from the corresponding author.

The 41-item baseline module was administered to patients at day 0 of the study, prior to treatment injection. Baseline module items can be categorized into four sections: disease and treatment background; direct impact on medical and non-medical resource utilization; indirect impact on employment and productivity; and intangible (humanistic) impacts. For example, treatment background and direct impact items assess treatments previously received and the perceived effectiveness and satisfaction with these treatments. Indirect impact items assess the effect of hyperhidrosis on employment and productivity, daily time spent treating hyperhidrosis, and daily frequency of bathing and clothing changes because of hyperhidrosis. Intangible (humanistic) impact items assess the emotional impact of hyperhidrosis and limitations in daily life and leisure activities due to hyperhidrosis. The HHIQ disease background items (e.g. disease history, hyperhidrosis triggers) were excluded from patient completion in this study because similar items were included as part of the medical history collected at the study screening visit.

The 10-item module of the HHIQ for follow-up assessment and comparison with baseline was completed by patients at the scheduled week 1, 4, 8, 12 and 16 study visits. These follow-up items focus mainly on indirect and intangible (humanistic) impacts of hyperhidrosis, as previously discussed.

In addition to the HHIQ, the SF-12 questionnaire was completed by patients on day 0, prior to treatment injection, and again at the week 16 study visit. The SF-12 is a validated, general health-related QOL questionnaire consisting of 12 items designed to assess patients' views about their general health, physical activity, emotional health, bodily pain and social functioning.¹⁸ Results are reported as physical component summary (PCS) and mental component summary (MCS) scores.

Statistical analysis

A target sample size of 300 patients for this study was based on the primary clinical end-point: the incidence of treatment responders at week 4. The assumptions for this target sample size included a

patient dropout rate of less than 10%, two-sided significance of 5%, and a power of 93% to detect a 25 percentage point difference between treatment groups (i.e. 60% and 35% for the BTX-A and placebo groups, respectively). This study was not powered to assess the patient questionnaires.

Descriptive statistics were reported for the baseline administration for all study subjects (i.e. BTX-A and placebo patients combined). Two sets of statistical analyses were performed. First, independent between-group comparisons were made at each time point for the BTX-A vs. the placebo groups. Second, within-group comparisons were conducted between the baseline visit and the end of the study. All between-group comparisons were conducted using a χ^2 test and all within-group comparisons used a Wilcoxon matched-pairs signed-rank test. No corrections were made for multiple comparisons. For items with multiple response options, the incidence of positively indicated responses was calculated. For some items, multiple responses were permitted. Confidence intervals were calculated based on the standard error of the proportion, and assessed using a χ^2 test. In addition, for some items regarding patient satisfaction, emotional effect of symptoms, and effect of symptoms on daily activities, a mean score for each group was calculated. In each analysis, n is the number of patients who answered the item. $P \leq 0.05$ was considered statistically significant for all analyses.

Results

Patient population

Patient flow through the study is illustrated in Figure 1. Between 27 April 1999 and 6 March 2000, 320 hyperhidrosis patients were randomized to receive either BTX-A ($n = 242$) or placebo ($n = 78$). Thirteen patients (eight in the BTX-A group and five in the placebo group) withdrew prior to the end of the study. Most of the patients who discontinued treatment were lost to follow-up or were withdrawn for other, primarily administrative, reasons.

There was no significant difference between the treatment groups receiving BTX-A or placebo with regard to any demographic variable (Table 1).

At baseline, in addition to axillary hyperhidrosis excessive non-axillary sweating was reported in the following locations by patients in the BTX-A and placebo groups, respectively: palms (47.1% vs. 48.7%), soles (40.9% vs. 35.9%), face (26.4% vs. 24.4%),

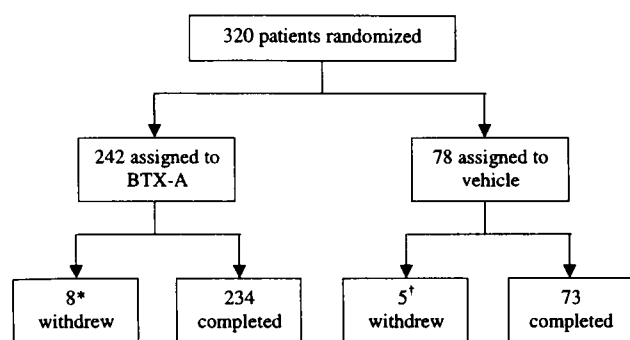


Figure 1. Patient flow through the study. *One patient withdrew because of an adverse event (not treatment-related); four were lost to follow-up; three withdrew for other reasons. †One patient was lost to follow-up; four withdrew for other reasons. 'Other' included non-compliance, failure to maintain visit schedule, patient request, or use of other, prohibited, hyperhidrosis therapies.

Table 1. Patient demographics

	BTX-A, no. (%) (n = 242)	Placebo, no. (%) (n = 78)
Mean age (years)	32	31
Range	17–74	18–58
Sex		
Male	113 (47)	35 (45)
Female	129 (53)	43 (55)
Mean weight (kg)	73	71
Range	44–124	49–100
Race		
Caucasian	237 (97.9)	77 (98.7)
Black	1 (0.4)	0
Asian	1 (0.4)	0
Other	3 (1.2)	1 (1.3)

BTX-A, botulinum toxin type A.

genitalia (16.5% vs. 20.5%) and other (20.6% vs. 29.5%). There were no significant differences between the two groups with regard to non-axillary sweating.

Treatment history and satisfaction

At baseline, many patients reported having used antiperspirants (308 of 318; 96.9%), systemic prescription medication (149 of 307; 48.5%) or herbal medicines (120 of 317; 37.9%) for their hyperhidrosis. A smaller number had prior experience with iontophoresis (41 of 305; 13.4%) or botulinum toxin injections (eight of 313; 2.6%), or had undergone surgical sympathectomy of the sweat glands (nine of 313; 2.9%). In addition, 49 of 303 (16.2%) patients had used antidepressants or anxiolytics; one-third of these

(16 of 49) reported that hyperhidrosis was the main reason why the medication was prescribed.

Patients were asked to rate the effectiveness of treatments they had previously used for hyperhidrosis. All the main treatments (antiperspirants, systemic prescription drugs, herbal products and iontophoresis) reported at baseline were considered by most of the patients to have poor effectiveness or not to be at all effective (Table 2). A large percentage of patients reported they had stopped using these treatments: antiperspirants (205 of 308; 66.6%), prescription drugs (104 of 149; 69.7%), herbal products (116 of 129; 96.7%), iontophoresis (35 of 41; 85.4%). The most frequently mentioned reasons for stopping treatment were lack of efficacy or adverse effects (Table 3).

Satisfaction with current and previous treatments for hyperhidrosis was further queried with two similar items. In the first item, patients were asked to describe their satisfaction with current treatment at baseline and throughout the study. At baseline, they described the treatment(s) they had used prior to entering the study, and a fairly low percentage in both treatment groups reported being somewhat or very satisfied (BTX-A, 31.7%; placebo, 20%) with that treatment. Following injection with study medication, the percentage of patients in the placebo group who were satisfied with their treatment increased to 47% at week 1 and then fell to 30.4% by week 16. In the BTX-A group, satisfaction with current treatment increased to 89.4% at week 1 and remained above 93% throughout the rest of the study. In the second item, patients were asked to compare their current study treatment directly with their previous treatment. The percentage of patients who reported being much more or somewhat more satisfied with their current treatment than with their previous treatment followed a similar pattern to the post-treatment satisfaction rates reported for the first item. These results are illustrated in Figure 2.

Time spent and activities involved in treating hyperhidrosis

At baseline, 151 of 242 (62.3%) patients in the BTX-A group and 40 of 78 (52%) patients in the placebo group reported spending only 15 min or less per day treating their hyperhidrosis. Following treatment, this percentage was significantly greater in the BTX-A group than the placebo group at every follow-up visit ($P \leq 0.001$). In the BTX-A group, the percentage of patients spending less than 15 min per day treating

Table 2. Effectiveness of prior treatment

Treatment	Effectiveness				
	Very good, no. (%)	Good, no. (%)	Average, no. (%)	Poor, no. (%)	Not effective, no. (%)
Antiperspirants (<i>n</i> = 305)	0	7 (2.3)	33 (10.8)	99 (32.5)	166 (54.4)
Prescription drugs ^a (<i>n</i> = 62)	0	3 (4.8)	10 (16.1)	18 (30.0)	31 (50.0)
Herbal/plant/organic medicines (<i>n</i> = 116)	0	2 (1.7)	7 (6.0)	24 (20.7)	83 (71.6)
Iontophoresis (<i>n</i> = 38)	1 (2.6)	2 (5.3)	8 (21.1)	14 (36.8)	13 (34.2)
BTX-A (<i>n</i> = 8)	3 (37.5)	2 (25)	1 (12.5)	2 (25)	0

BTX-A, botulinum toxin type A. *n*, the number of subjects who used each treatment and rated its effectiveness.

^aPrescription drug effectiveness was based on use in the preceding 3 months.

Table 3. Reasons for stopping prior treatment^a

	Lack of effect, no. (%)	Side-effects, no. (%)	Cost, no. (%)	Time to use, no. (%)	Other, no. (%)	Total reasons, no.
Antiperspirants	184 (79.3)	28 (12.1)	6 (2.6)	3 (1.3)	11 (4.7)	232
Prescription medication	63 (52.5)	38 (31.7)	4 (3.3)	0	15 (12.5)	120
Herbal medicines	110 (86.6)	3 (2.4)	7 (5.5)	5 (3.9)	2 (1.6)	127
Iontophoresis	29 (67.4)	4 (9.3)	1 (2.3)	7 (16.3)	2 (4.7)	43

^aMultiple responses were permitted. The denominator is the total number of reasons mentioned.

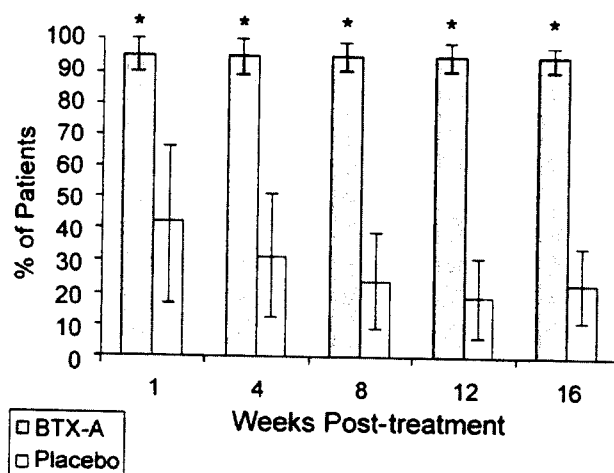


Figure 2. Percentage of patients much more, or somewhat more, satisfied with their current treatment than their previous treatment. †Response to question: Compared with treatments you have used for hyperhidrosis before this study, how satisfied are you overall with this study treatment? (Hyperhidrosis Impact Questionnaire[®]) Response options: much more satisfied, somewhat more satisfied, neutral, somewhat less satisfied, much less satisfied. Bar height indicates group mean values. Error bars indicate the upper and lower bounds of the 95% confidence interval. BTX-A, botulinum toxin type A. **P* < 0.001 compared with placebo.

their hyperhidrosis increased to 82.5% at week 1, remained above 85% through week 12, and was 78.8% at week 16 post-treatment.

Following treatment, the percentage of patients changing clothing (Fig. 3) multiple times per day decreased in the BTX-A group and remained significantly lower than the percentage in the placebo group at all follow-up visits (*P* ≤ 0.001). For most of the follow-up period, fewer than 10% of patients in the BTX-A group had to change their clothing two or more times per day, significantly lower than the placebo group.

Impact of hyperhidrosis on daily life

At baseline, large numbers of patients reported that hyperhidrosis had a negative impact on several aspects of their daily lives (Table 4).

Patients also rated the degree of limitation caused by hyperhidrosis with respect to being in public places, meeting people for the first time, spending time with family and friends, developing personal relationships, engaging in sexual activities, or participating in sports. They also rated the emotional impact of their hyperhidrosis. In all cases, the degree of limitation was moderate at baseline and similar between the two treatment groups. Following treatment, the limitations resulting from hyperhidrosis were significantly less in the BTX-A group than in the placebo group at all follow-up visits (*P* ≤ 0.01).

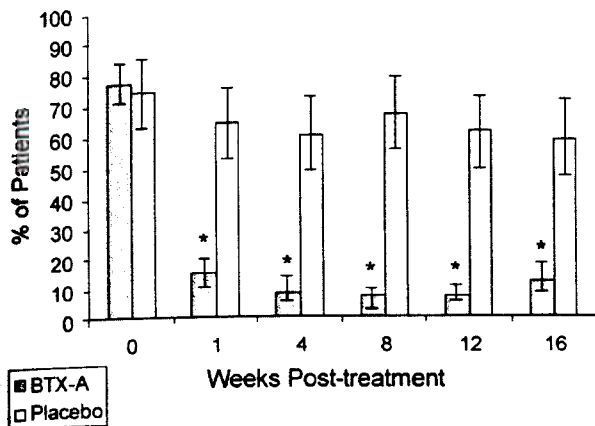


Figure 3. Percentage of patients who indicated that they changed clothing two or more times per day as a result of their hyperhidrosis. *Response to question: How frequently must you currently change your shirt or other clothes due to the effects of your hyperhidrosis? (Hyperhidrosis Impact Questionnaire[®]) Response options: I can wear my clothing for several days, daily, twice per day, three times or more per day. Bar height indicates group mean values. Error bars indicate the upper and lower bounds of the 95% confidence interval. BTX-A, botulinum toxin type A. * $P < 0.001$ compared with placebo.

Table 4. Effect of hyperhidrosis on daily life and activities ($n = 320$)

My hyperhidrosis has caused me to...	Patients, no. (%) ^a
Feel less confident than I would like	227 (71.8)
Feel unhappy or depressed	154 (48.7)
Change the types of leisure activities I pursue	141 (44.6)
Become frustrated with many daily activities	96 (30.4)
Miss outings or events with friends or family	79 (25.0)
Decrease amount of time spent on leisure activities	61 (19.3)

^aNumber (and percentage) of patients who indicated that the above statements were true.

At baseline, the percentage of patients reporting that they were at least moderately limited ranged from 11.8% (with regard to sexual activities) to 80.5% (with regard to meeting people for the first time). Following treatment, the percentage of patients reporting that they were at least moderately limited dropped markedly in the BTX-A group for all measures of daily activities, and remained low throughout the study. In contrast, there was very little change in the placebo group. The most dramatic changes were seen in the degree of limitation on being in public places and on meeting people for the first time. For both of these measures, there was a high degree of limitation at baseline that was markedly improved by BTX-A treatment (Figs 4 and 5).

At baseline, the overwhelming majority of patients in both treatment groups reported that their emotional

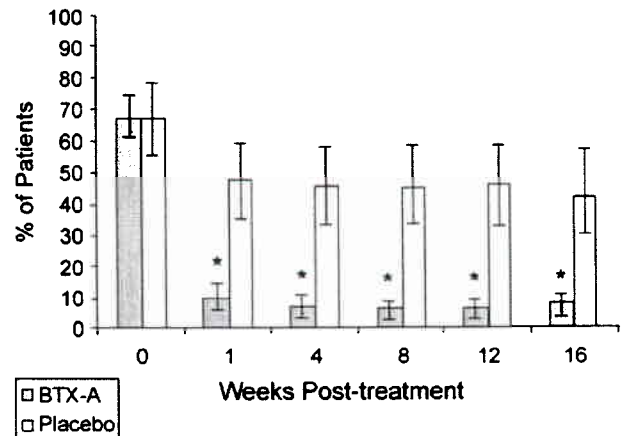


Figure 4. Percentage of patients who reported feeling at least moderately limited in public places as a result of their hyperhidrosis. *Response to question: How limited do you feel you currently are in each of these activities/situations due to your hyperhidrosis: being in public places? (Hyperhidrosis Impact Questionnaire[®]) Response options: not limited, somewhat limited, moderately limited, quite a bit limited, extremely limited. Bar height indicates group mean values. Error bars indicate the upper and lower bounds of the 95% confidence interval. BTX-A, botulinum toxin type A. * $P < 0.001$ compared with placebo.

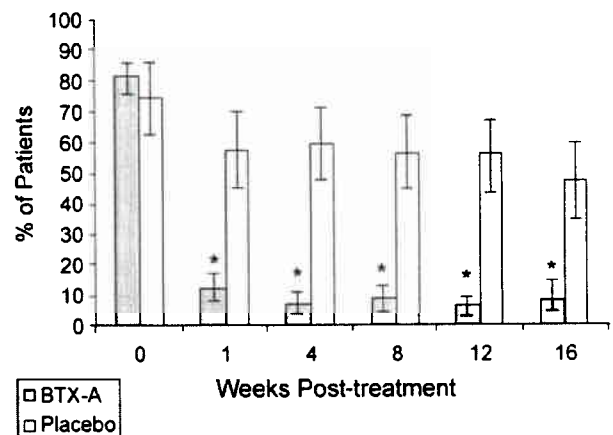


Figure 5. Percentage of patients who reported feeling at least moderately limited as a result of their hyperhidrosis when meeting people for the first time. *Response to question: How limited do you feel you currently are in each of these activities/situations due to your hyperhidrosis: when meeting or being introduced to people for the first time? (Hyperhidrosis Impact Questionnaire[®]) Response options: not limited, somewhat limited, moderately limited, quite a bit limited, extremely limited. Bar height indicates group mean values. Error bars indicate the upper and lower bounds of the 95% confidence interval. BTX-A, botulinum toxin type A. * $P < 0.001$ compared with placebo.

status was affected to at least some degree by hyperhidrosis (Fig. 6). Over one-quarter of patients reported being moderately affected (BTX-A, 27.5%; placebo, 22.1%) and almost one-third reported being

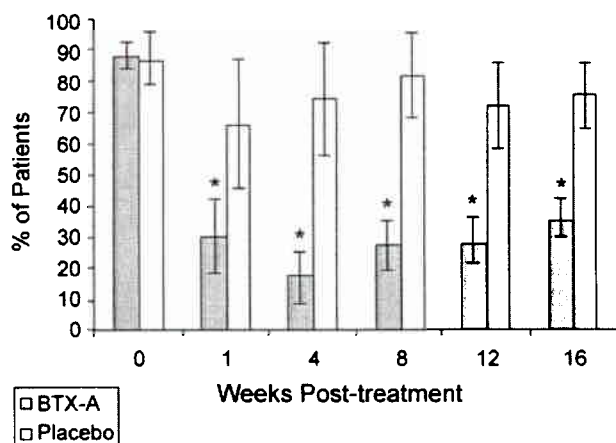


Figure 6. Percentage of patients who reported any effect of hyperhidrosis symptoms on their emotional status. *Response to question: Do you currently feel emotionally damaged/injured by your hyperhidrosis? (Hyperhidrosis Impact Questionnaire[®]) Response options: not affected emotionally, affected emotionally to a small extent, moderately affected emotionally, significantly affected emotionally. Bar height indicates group mean values. Error bars indicate the upper and lower bounds of the 95% confidence interval. BTX-A, botulinum toxin type A. * $P < 0.001$ compared with placebo.

significantly affected (BTX-A, 32.2%; placebo, 28.6%). Following treatment, the negative impact of hyperhidrosis on emotional status was significantly less in the BTX-A group than in the placebo group at all follow-up visits ($P \leq 0.001$). Placebo treatment had very little effect on emotional status.

Impact on employment and productivity

Although patients did not report significant absences from work due to hyperhidrosis, many indicated that they considered their performance and productivity while at work to be affected. At baseline, less than one-fifth of patients in either group considered themselves either somewhat satisfied or very satisfied with their ability to perform their current work activities. After treatment, the satisfaction rate in the BTX-A group increased markedly and was significantly higher than in the placebo group at every follow-up visit ($P \leq 0.001$; Fig. 7).

Impact on general quality of life: Short Form-12

There was a statistically significant improvement in QOL as measured by the SF-12 in both the PCS score and the MCS score in BTX-A-treated patients. Changes in the placebo group were not statistically significant.

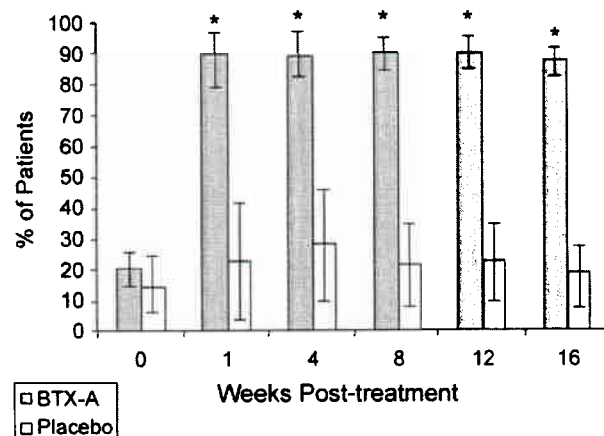


Figure 7. Percentage of patients who reported being very satisfied or somewhat satisfied in their ability to perform current work activities. *Response to question: Please rate your overall level of satisfaction with each of the following: your ability to perform your current work activities, as a result of your hyperhidrosis. (Hyperhidrosis Impact Questionnaire[®]) Response options: very satisfied, somewhat satisfied, neutral, somewhat dissatisfied, very dissatisfied, does not apply to me. Bar height indicates group mean values. Error bars indicate the upper and lower bounds of the 95% confidence interval. BTX-A, botulinum toxin type A. * $P < 0.001$ compared with placebo.

At baseline, the PCS of the SF-12 showed no difference between the two treatment groups ($P = 0.197$), with mean scores of 52.2 in the BTX-A group and 52.8 in the placebo group. At the end of the study, the mean score had significantly improved from baseline by 0.9 in the BTX-A group ($P = 0.012$) and decreased by 1.2 in the placebo group ($P = 0.221$). The difference in change from baseline between the two treatment groups was statistically significant ($P = 0.019$).

For the MCS of the questionnaire, the subjects in the BTX-A group had a significantly higher score compared with the placebo group at baseline (49.1 and 46.4, respectively, $P = 0.023$). At the end of the study, the mean score had significantly improved by 1.7 in the BTX-A group ($P = 0.013$) and by 0.5 in the placebo group ($P = 0.890$). The difference in change from baseline between the two treatment groups was not statistically significant ($P = 0.247$).

Safety

The clinical results of this trial, including safety findings, have been described in detail elsewhere.¹³ In summary, most adverse events were mild or moderate and were similar between the treatment groups in type, incidence and severity.

Discussion

This study shows that BTX-A treatment for axillary hyperhidrosis resulted in greater improvements in QOL than did placebo. In particular, treatment of axillary hyperhidrosis with BTX-A led to a marked improvement in emotional status, ability to participate in many aspects of daily life and social activities, and in satisfaction with productivity at work. These improvements were substantial, observed within 1 week of treatment, and were sustained with little or no decline throughout the 16-week follow-up period. The superiority of BTX-A treatment over placebo was observed on the HHIQ follow-up module items and for the PCS of the SF-12. Moreover, it was observed from the HHIQ baseline items related to treatment history and satisfaction that BTX-A resulted in a greater level of overall satisfaction than many other treatments.

These results confirm previous research that documented the substantial QOL burden on patients with hyperhidrosis and that QOL can be substantially improved with BTX-A treatment.¹²⁻¹⁴ For example, Swartling *et al.* administered the Dermatology Life Quality Index (DLQI) to 53 patients before and after treatment with BTX-A for severe focal hyperhidrosis of the axillary, palmar or plantar locations (treatment was to either one or a combination of these locations).¹⁴ The QOL burden to these hyperhidrosis patients as measured by a mean DLQI score of 10.1 was observed to be of similar or greater magnitude than that reported for other dermatological conditions, including severe acne (mean DLQI score = 9.2) and psoriasis (mean DLQI score = 8.9). Furthermore, Swartling *et al.* demonstrated that treatment with BTX-A resulted in a clinically meaningful improvement in QOL (mean reduction in DLQI score from 9.9 to 2.4; $P < 0.0001$) for patients ($n = 35$) who had not relapsed at a median of 5 months (range 2-10) post-BTX-A treatment. For eight patients treated only for axillary hyperhidrosis and who did not have a relapse at a median of 4.4 months (range 2-8) post-BTX-A treatment, the mean DLQI score was reduced from 11.6 to 2.4.

The results of the present study go beyond previous findings by demonstrating that hyperhidrosis has an impact on satisfaction with work activities, and showing that a relatively simple, minimally invasive procedure (BTX-A injections) resulted in marked improvements in satisfaction with work activities, as well as in a broad range of other QOL parameters. The study design also allowed for the robust evaluation of

the BTX-A treatment effect on QOL compared with that of placebo. In addition, the study is unique in that it included administration of a new hyperhidrosis-specific QOL questionnaire to a large, homogeneous population (primary axillary focal hyperhidrosis) enrolled in a randomized, double-blind, placebo-controlled trial. It provides a comprehensive assessment of the impact of axillary hyperhidrosis and the value of treatment by addressing a broader and more disease-relevant scope of items, compared with items included in either general or dermatology-specific QOL questionnaires.

Questionnaire administration at baseline and at multiple post-treatment visits (i.e. weeks 1, 4, 8, 12 and 16) could have resulted in poor item response rates and recall bias and, thus, could be a potential limitation of the current research. For example, in a review on QOL measurement in dermatology, Finlay reported that more than three administrations of a questionnaire may be too frequent and may yield decreased interest by patients to complete the questionnaires and increase recall of previous answers.¹⁹ In the present study, questionnaire administration at baseline and post-treatment coincided with scheduled office visits and clinical assessments, allowing assessment of both the onset and duration of treatment effect compared with placebo vehicle treatment. High response rates were observed at all time points, suggesting that the questionnaire administration was not so frequent as to decrease the response rate. However, the potential for recall bias remains and cannot be directly measured.

The improvements in the PCS score of the SF-12 survey following BTX-A treatment were interesting, but they were small and their clinical relevance still needs to be assessed. Because the SF-12 is not disease-specific, it would not be expected to be as sensitive as the HHIQ follow-up items to disease-specific changes in QOL during the short time period of the clinical trial. Furthermore, review of the medical literature found no publications in dermatology using the SF-12. Additional long-term studies with a larger patient population are needed to determine the clinical relevance of the SF-12 finding.

To permit a comparison of the effects of BTX-A injections with other hyperhidrosis treatments (such as antiperspirants, iontophoresis and systemic prescription drugs), more information is needed about the QOL benefits of these other treatments. Our research does show, however, that patients in the population studied do not consider the latter treatments to be very

effective. The extent to which this observation can be generalized to other patients suffering from axillary hyperhidrosis is a suitable area for future research. Studies have documented that ETS is effective and does improve the QOL of hyperhidrosis patients.^{1,3} ETS can be associated with several adverse effects, including a very high rate of compensatory hyperhidrosis³⁻⁶ (in axillary patients), and approximately 20% of axillary hyperhidrosis patients report dissatisfaction with the results of this procedure.^{4,5} Information about other surgical approaches, such as subcutaneous curettage and liposuction, is currently too limited to support a well-founded benefit-risk consideration. Compared with surgery, BTX-A treatment is also highly effective,^{12-14,20} and has a long and excellent safety profile¹³ spanning a wide range of applications, and as demonstrated in our study, a very high level of satisfaction (more than 90%) among patients with hyperhidrosis.

It should be noted that the results reported in this study are based on the Botox[®] formulation of BTX-A and cannot be generalized to other formulations of BTX-A or to other botulinum toxin serotypes.

In conclusion, the results of the present study demonstrate that chronic hyperhidrosis has a significant negative impact on QOL and that the lives of patients with this disabling condition can be markedly improved by BTX-A treatment.

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