

Functional and Dermatology-Specific Quality of Life Benefits With Repeated Botulinum Toxin Type A Treatment of Primary Axillary Hyperhidrosis Over 4 Years

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INTRODUCTION

Primary axillary hyperhidrosis is a chronic disorder of excessive underarm sweating that causes significant impairment of an individual's work productivity, daily activities, emotional well-being, and personal relationships.^{1,3} The marked reduction in dermatology-specific quality of life (DSQOL) associated with hyperhidrosis is similar to or greater than that with other serious dermatologic diseases, such as psoriasis and severe acne.^{3,6} Clinical studies in populations in Europe and North America have shown that, in addition to significantly reducing sweat production,^{2,7,8} botulinum toxin type A (BoNTA) improves DSQOL and reduces the limitations on daily activities that are associated with the disorder.^{1,2,5,9-11} The long-term effect of BoNTA treatment on DSQOL has not been established, however, because only 1 study has evaluated the durability and reproducibility of these improvements over the period of a year.¹⁰ Here we report the combined results of the 1-year study and a subsequent 3-year open-label extension study that was designed to quantify the effects of repeated treatment with BoNTA on DSQOL and daily functioning in patients with primary axillary hyperhidrosis.

METHODS

Patients who completed the 1-year double-blind randomized controlled trial (RCT), regardless of treatment arm (BoNTA 50 U per axilla, BoNTA 75 U per axilla, or placebo) were eligible for a subsequent 3-year open-label extension trial with BoNTA 50 U per axilla. In the extension trial patients were assessed during a telephone visit 7 days post-treatment, at office visits 4 and 8 weeks post-treatment, and during monthly telephone visits thereafter until they were eligible for retreatment or exited the study. Patients were eligible for retreatment 8 weeks after their last treatment if their symptoms persisted or recurred. The retreatment criteria were (1) a score of 3 or 4 on the Hyperhidrosis Disease Severity Scale (HDSS; range, 1-4), indicating that their underarm sweating was barely tolerable or intolerable and frequently or always interfered with their daily activities; and (2) a gravimetric measurement of at least 50 mg of spontaneous sweat in each axilla over 5 minutes at rest.

The primary efficacy measure was the score on the HDSS, a validated single-item 4-point scale on which a higher score indicates greater interference with daily activities due to hyper-

hidrosis.¹² The duration of response was calculated as the number of days after each BoNTA treatment to the first reporting of a score of 3 or 4 on the HDSS (or discontinuation from the study).

Daily functioning and DSQOL were assessed by using the Dermatology Life Quality Index (DLQI) and the Hyperhidrosis Impact Questionnaire (HHIQ). The DLQI is a validated and reliable 10-item dermatology-specific questionnaire that assesses DSQOL over the previous week,¹³ with total scores ranging from 0 to 30 (0 being the least impaired DSQOL and 30 being the most impaired). The HHIQ is a validated and reliable 41-item instrument that quantifies functional impairment in terms of occupational and personal limitations due to hyperhidrosis, as well as the time spent managing it.^{9,14} The HHIQ is administered as a 41-item questionnaire at baseline and as a shortened, 10-item questionnaire at follow-up visits. Patients completed both the DLQI and the HHIQ at each office visit before treatment and 4 and 8 weeks after each treatment.

This analysis summarizes the combined data from the 1-year RCT and the 3-year open-label extension study. For the DLQI total score, descriptive statistics were calculated for each treatment session and within-group changes from baseline were analyzed by using the Wilcoxon signed-rank test. Responses to selected HHIQ questions were dichotomized and summarized with frequency distributions. Within-group comparisons were made by using the McNemar test. A *P* value of ≤ 0.05 was considered statistically significant. All analyses were based on observed cases, and no data imputation was performed.

RESULTS

One hundred ninety-three of 252 patients enrolled in the open-label study after completing the 1-year RCT. Of the patients who received BoNTA treatment during the 4 years of follow-up, 186 received at least 1 treatment, 140 received at least 2 treatments, 104 received at least 3 treatments, 67 received at least 4 treatments, and 43 received at least 5 treatments. Results for the first 5 BoNTA treatment sessions are presented, as only 16% of patients (30/193) received more than 5 treatments over 4 years. Patient demographics are reported in Table 1.

Table 1. Demographics

Characteristic	Treated population (n = 186)
Age, y, mean (range)	33 (18–65)
Sex, %	
Male	51
Female	49
Ethnicity, %	
Caucasian	83
Non-Caucasian	17
Treatment assignment in RCT, %	
Placebo	19
BoNTA 50 U or 75 U per axilla	81

RCT, randomized controlled trial.

Efficacy

HDSS

- After initial BoNTA treatment (ie, treatment session 1), 82% (141/172) and 77% (131/170) of patients at 4 and 8 weeks, respectively, reported a ≥ 2 -point improvement in their HDSS score
 - The mean reduction in HDSS scores was 2.1 at week 4 and 2.0 at week 8
- BoNTA showed continued effectiveness with repeated treatment
- After treatment sessions 2, 3, 4, and 5, 82% (98/119), 85% (76/89), 80% (45/56), and 84% (32/38) of patients reported a ≥ 2 -point improvement in their HDSS score at 4 weeks, respectively
- The treatment effect was durable
 - The median duration of effect in patients with a ≥ 2 -point improvement in their HDSS score from baseline to week 4 was 232, 238, 223, 183, and 175 days in treatment sessions 1 through 5, respectively

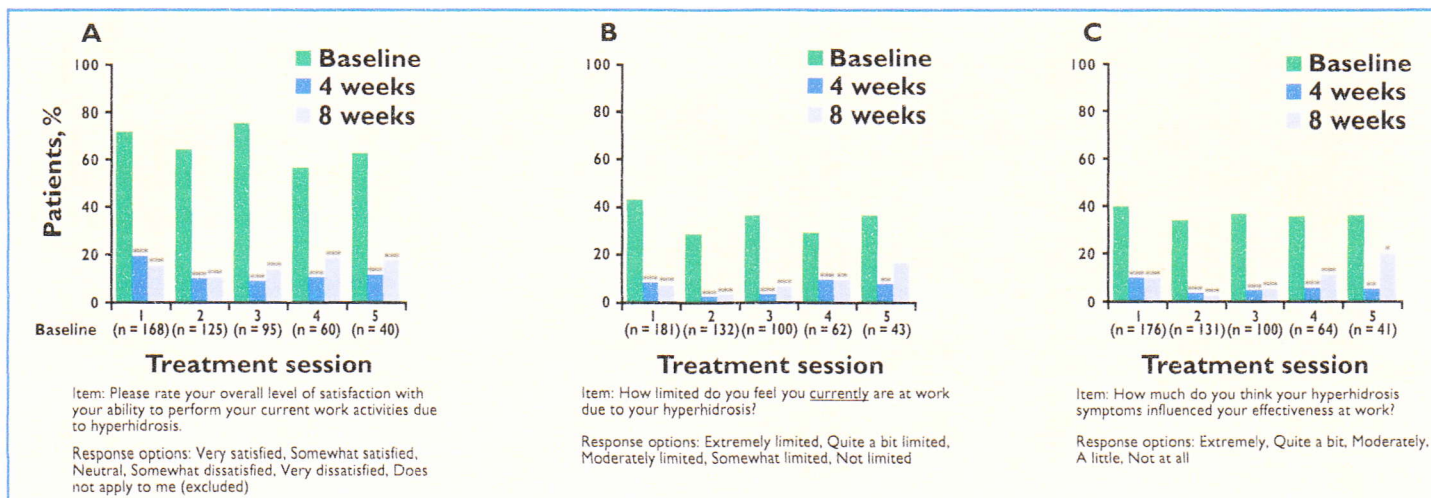


Figure 2. Occupational impairment before and after treatment with BoNTA. (A) Patients somewhat or very dissatisfied with their ability to perform their work activities because of hyperhidrosis; (B) Patients at least moderately limited at work because of hyperhidrosis; (C) Patients who reported that their hyperhidrosis at least moderately affected their effectiveness at work. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ vs baseline.

DSQOL Measurements

DLQI

- Significant improvements in DSQOL were reported after each BoNTA treatment (Figure 1A)
 - Mean total DLQI scores before each BoNTA treatment ranged from 5.9 to 8.5
 - Mean total DLQI scores at 4 and 8 weeks after each BoNTA treatment decreased to between 1.3 and 3.1 ($P < 0.001$ vs baseline)

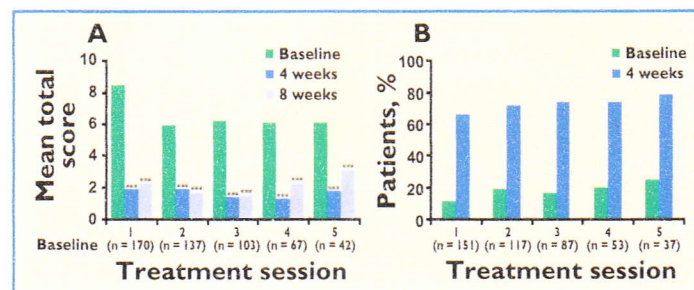


Figure 1. Dermatology-Specific Quality of Life (DSQOL) before and after treatment with BoNTA. (A) Mean DLQI total score; (B) Patients with a total DLQI score ≤ 1 . *** $P < 0.001$ vs baseline.

- After each treatment with BoNTA there was a substantial increase in the proportion of patients with a total DLQI score ≤ 1 , indicating no or minimal impairment of DSQOL, as is reported in individuals without dermatologic conditions (Figure 1B)
 - 11% to 24% of patients had a total DLQI score ≤ 1 before treatment with BoNTA
 - 66% to 78% of patients had a total DLQI score ≤ 1 after treatment with BoNTA
- At 4 weeks after each BoNTA treatment a majority of patients (71% to 82%) achieved a 5-point improvement in total DLQI score, indicating a clinically meaningful improvement in DSQOL

HIIQ

Occupational impairment

- Patients reported significantly less occupational dissatisfaction and limitations due to their hyperhidrosis after treatment with BoNTA than before treatment

- 57% to 76% of patients were neutral or somewhat or very dissatisfied with their ability to perform their work activities before treatment, which decreased to 9% to 20% of patients at 4 and 8 weeks after treatment ($P < 0.001$) (Figure 2A)
- 29% to 43% of patients reported being moderately, quite a bit, or extremely limited at work because of their hyperhidrosis before treatment, which decreased to 3% to 17% of patients at 4 and 8 weeks after treatment ($P < 0.01$ at all time points, except at week 8 of treatment session 5 [$P = 0.059$]) (Figure 2B)
- 34% to 40% of patients reported that their effectiveness at work was moderately, quite a bit, or extremely affected by their hyperhidrosis before treatment, which decreased to 3% to 20% of patients at 4 and 8 weeks after treatment ($P < 0.05$) (Figure 2C)

Time spent managing symptoms

- Patients reported that they spent significantly less time treating their hyperhidrosis and changed their clothing less often after treatment with BoNTA than before treatment (Figure 3)
 - 31% to 40% of patients spent an average of 15 minutes or more on the previous day treating their hyperhidrosis before treatment, which decreased to 7% to 17% at 4 and 8 weeks after treatment ($P < 0.01$ at all time points, except at week 8 of treatment session 5 [$P = 0.059$]) (Figure 3A)
 - 26% to 54% of patients changed their shirt or other clothing 2 or more times on the previous day before treatment, which decreased to 6% to 12% at 4 and 8 weeks after treatment ($P < 0.01$ at all time points, except at week 8 of treatment session 5 [$P = 0.083$]) (Figure 3B)

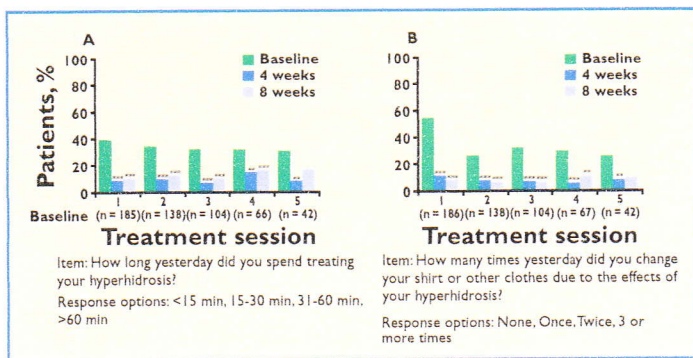


Figure 3. Time spent managing symptoms before and after treatment with BoNTA. (A) Patients who spent 15 minutes or more the previous day treating their hyperhidrosis; (B) Patients who changed their clothing at least twice the previous day because of hyperhidrosis. ** $P < 0.01$; *** $P < 0.001$ vs baseline.

Psychological impairment

- Significantly fewer patients reported feeling emotionally damaged or injured because of their hyperhidrosis after treatment than before treatment (Figure 4)
 - 69% to 83% of patients felt emotionally damaged or injured because of their hyperhidrosis before treatment
 - 34% to 47% of patients felt emotionally damaged or injured because of their hyperhidrosis at 4 and 8 weeks after treatment ($P < 0.05$)

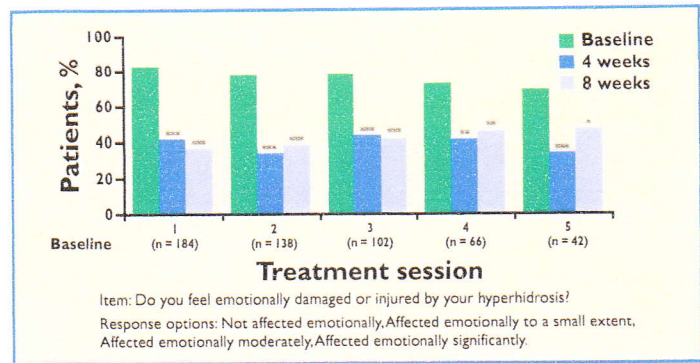


Figure 4. Psychologic impairment before and after treatment with BoNTA. Patients who felt emotionally damaged or injured, at least to a small extent, because of their hyperhidrosis. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ vs baseline.

Limitations in interpersonal and social situations

- Patients reported significantly less limitations in interpersonal and social situations because of their hyperhidrosis after treatment than before treatment (Figure 5)
 - 20% to 35% of patients felt at least moderately limited with family or with friends before treatment, which decreased to 1% to 7% at 4 and 8 weeks after treatment ($P < 0.01$) (Figure 5A)
 - 38% to 58% of patients felt at least moderately limited in meeting or being introduced to new people before treatment, which decreased to 6% to 17% at 4 and 8 weeks after treatment ($P < 0.001$) (Figure 5B)
 - 33% to 55% of patients felt at least moderately limited in public places before treatment, which decreased to 3% to 11% at 4 and 8 weeks after treatment ($P < 0.001$) (Figure 5C)
 - 66% to 83% of patients were neutral, somewhat dissatisfied, or very dissatisfied with their ability to perform nonwork activities (social and leisure) before treatment, which decreased to 11% to 22% at 4 and 8 weeks after treatment ($P < 0.001$) (Figure 5D)
 - Other interpersonal and social variables that were extremely limited by hyperhidrosis but that significantly improved after BoNTA treatment included shaking hands, developing personal relationships, and participating in sexual activities and in sports

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Notes

The dosing and results reported in this study are specific to the formulation of botulinum toxin type A manufactured by Allergan, Inc (Irvine, Calif). The Allergan, Inc, formulation is not interchangeable with other botulinum toxin products and cannot be converted by using a dose ratio.

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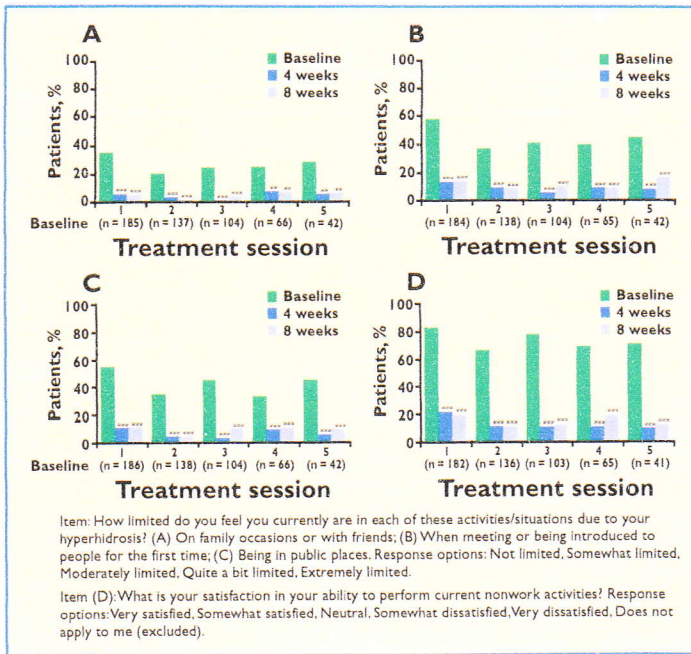


Figure 5. Limitations in interpersonal and social situations before and after treatment with BoNTA. (A) Patients who felt at least moderately limited at family occasions or with friends because of hyperhidrosis; (B) Patients who felt at least moderately limited when meeting or being introduced to new people because of hyperhidrosis; (C) Patients who felt at least moderately limited in public places because of hyperhidrosis; (D) Patients who were neutral, somewhat, or very dissatisfied with their ability to perform nonwork (social and leisure) activities because of hyperhidrosis. **P < 0.01, ***P < 0.001 vs baseline.

CONCLUSIONS

- Patients with primary axillary hyperhidrosis have substantial DSQOL impairment because of their condition
- BoNTA treatment significantly improves DSQOL
 - Impairments in daily activities, work, and a range of social interactions that were due to primary axillary hyperhidrosis were significantly reduced, as measured by the HHIQ at weeks 4 and 8 post-treatment
 - The majority of patients (66%–78%) achieved a total DLQI score of 0 or 1 after treatment with BoNTA, indicating that DSQOL impairment was either eliminated or reduced to a minimal level, similar to that of individuals without dermatologic conditions
- Repeated BoNTA treatment over 4 years resulted in consistent, reproducible, and meaningful benefits in patients with primary axillary hyperhidrosis