

Effect of Repeated Botulinum Toxin Type A Treatment on Health-Related Quality of Life and Functioning in Patients With Primary Axillary Hyperhidrosis: Results From 2 Years of Longitudinal Data

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INTRODUCTION

Primary axillary hyperhidrosis, a chronic pathologic condition of excessive underarm sweating, causes significant occupational impairment and difficulties in personal relationships, and requires substantial time and effort to manage.^{1,2} The marked reduction in health-related quality of life (HRQOL) associated with hyperhidrosis is similar to or greater than that with other serious dermatologic diseases, such as psoriasis and severe acne.^{4,4} Clinical studies have shown that botulinum toxin type A significantly reduces sweat production in patients with hyperhidrosis.^{5,7,8} However, because this condition is associated with substantial impairment in daily activities, evaluating the efficacy of treatment also requires assessing its effects with HRQOL measures.

Studies in Canadian, European, and North American populations have shown that, in addition to reducing sweat production, treatment with botulinum toxin type A (BoNTA) improves HRQOL and associated limitations in daily activities.^{1-3,5,9,10} Only 1 of these studies,¹⁰ however, assessed the effects of botulinum toxin type A therapy on HRQOL over an extended time period (1 year). Here we report the interim results of an open-label extension of that 1-year study. This report quantifies the effects of repeated treatment with BoNTA on HRQOL and daily functioning in patients with primary axillary hyperhidrosis over a 2-year period.

METHODS

Patients who completed the 1-year double-blind randomized clinical trial (RCT), regardless of treatment group (BoNTA 50 U/axilla, BoNTA 75 U/axilla, or placebo), were eligible for a subsequent 3-year open-label extension trial with BoNTA 50 U/axilla. In the open-label extension trial patients were assessed during a telephone visit 7 days post-treatment, at office visits at 4 and 8 weeks post-treatment, and during monthly telephone visits thereafter until they were eligible for reinjection 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; Table 1), 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 measurement was the HDSS, a validated single-item 4-point scale in which the patient rates the degree of interference of his or her hyperhidrosis symptoms with his or her daily activities.¹¹ A higher score indicates greater interference with

daily activities. 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).

Table 1. Hyperhidrosis Disease Severity Scale

Question: How would you rate the severity of your hyperhidrosis?	Score
My underarm sweating is never noticeable and never interferes with my daily activities	1
My underarm sweating is tolerable but sometimes interferes with my daily activities	2
My underarm sweating is barely tolerable and frequently interferes with my daily activities	3
My underarm sweating is intolerable and always interferes with my daily activities	4

Daily functioning and HRQOL 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 HRQOL over the previous week,¹² with total scores that range from 0 to 30 (0 being the least impaired HRQOL and 30 being the most impaired). The HHIQ is a validated and reliable instrument that quantifies functional impairment in terms of occupational and personal limitations due to hyperhidrosis, as well as the time spent managing it.^{9,13} Patients completed both instruments before each treatment and 4 and 8 weeks thereafter.

This analysis is of data from the RCT (1 year) combined with 1 year of data from the 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.

RESULTS

77% (193/252) of patients who completed the 1-year RCT enrolled in the open-label study; 78% (150/193) had previously been randomized to treatment with BoNTA, the remaining 43 patients had previously received placebo. During the 2 years of follow-up 185 (96%) of these 193 patients had received at least 1 BoNTA treatment, 3 (2%) had completed or discontinued the open-label study without having received any BoNTA treatment,

and 5 (3%) were enrolled who had not received any BoNTA treatment. Of the patients who had received BoNTA treatment during the 2 years of follow-up, 34% (62/185) received 1 treatment, 30% (55/185) received 2 treatments, 21% (39/185) received 3 treatments, and 10% (18/185) received 4 treatments. Patient demographics are reported in Table 2.

Table 2. Demographics

Characteristic	Enrolled population (N = 193)
Age, y, mean (range)	33 (18–65)
Sex, %	
Male	52
Female	48
Ethnicity, %	
White	84
Hispanic	9
Black	5
Other	2
Treatment in previous study, %	
Placebo	22
BoNTA 50 U or 75 U/axilla	78

Efficacy

HDSS

- 4 and 8 weeks after treatment session 1, 83% (41/171) and 78% (131/169) of patients, respectively, reported at least a 2-grade improvement from baseline on the HDSS
- The treatment effect was durable. After treatment session 1 the median duration of effect was 226 days in patients with at least a 2-grade decrease in HDSS score from baseline to week 4 (Figure 1). Repeated treatment with BoNTA showed continued effectiveness, as 81% (83/103) and 78% (40/51) of patients reported at least a 2-grade improvement in HDSS score from baseline at 4 weeks after treatment sessions 2 and 3, respectively
 - The median durations of effect were 225 and 179 days, respectively, in patients with at least a 2-grade decrease in HDSS score from baseline to week 4 after treatment sessions 2 and 3 (Figure 1)
 - The duration of treatment response is likely underestimated, particularly after treatment session 2, because the treatment was truncated in patients who continued to show a response to treatment

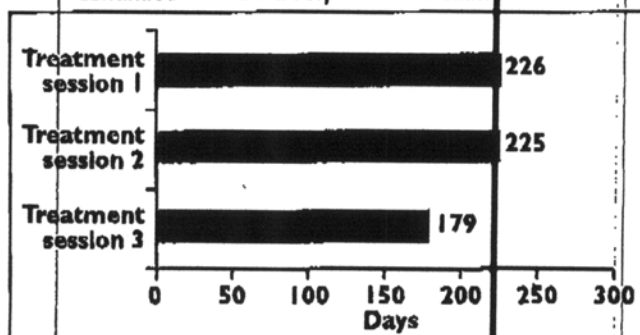


Figure 1. Median duration of treatment effect in patients with at least a 2-grade improvement from baseline in HDSS score at week 4.

HRQOL Measurements

- Significant improvements in dermatology-specific HRQOL were reported after each treatment with BoNTA (Figure 2)
 - Mean total DLQI scores before each BoNTA treatment ranged from 5.9 to 8.5 (Figure 2)
 - Mean total DLQI scores at 4 weeks after each BoNTA treatment ranged from 1.8 to 1.9 ($P < 0.001$)
 - Mean total DLQI scores at 8 weeks after treatment ranged from 1.5 to 2.3 ($P < 0.001$)

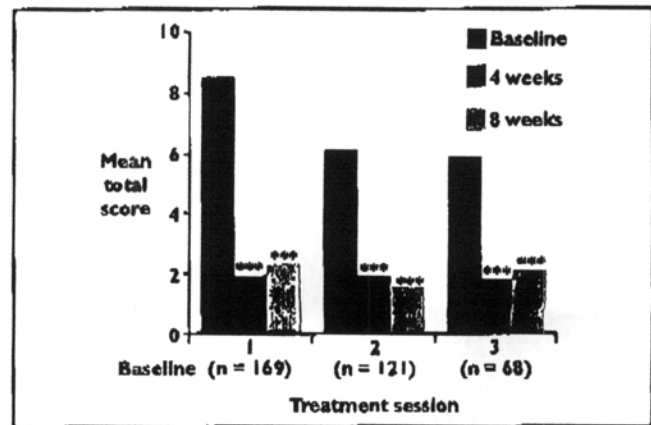


Figure 2. Dermatology-specific HRQOL, indicated by the mean DLQI total score before and after treatment with BoNTA. * $P < 0.001$ vs baseline.**

Occupational impairment

- Patients reported significantly less occupational dissatisfaction and limitations due to their hyperhidrosis after treatment with BoNTA than before treatment
 - 66%–72% of patients were neutral or somewhat or very dissatisfied with their ability to perform their work activities before treatment, which decreased to 9%–20% at 4 weeks after treatment ($P < 0.001$) (Figure 3A)
 - 29%–43% of patients reported being moderately, quite a bit, or extremely limited at work because of their hyperhidrosis before treatment, which decreased to 3%–8% at 4 weeks after treatment ($P < 0.001$) (Figure 3B)
 - 35%–41% of patients reported that their hyperhidrosis moderately, quite a bit, or extremely affected their effectiveness at work before treatment, which decreased to 4%–11% at 4 weeks after treatment ($P < 0.01$) (Figure 3C)

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
 - 31%–40% of patients spent an average of 15 minutes or more on the previous day treating their hyperhidrosis before treatment, which decreased to 6%–10% at 4 weeks after treatment ($P < 0.01$) (Figure 4A)
 - 29%–55% of patients changed their shirt or other clothing

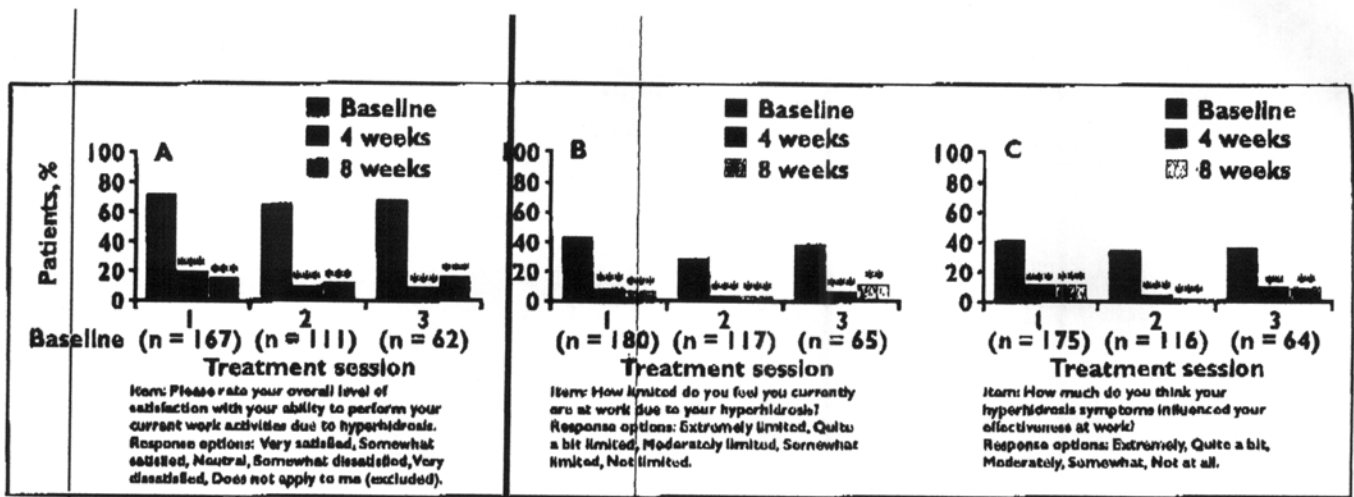


Figure 3. Occupational impairment before and after treatment with BoNTA. (A) Patients somewhat or very dissatisfied with their ability to perform their work activities because of hyperhidrosis; (B) Patients at least moderately limited at work because of hyperhidrosis; (C) Patients who reported that their hyperhidrosis at least moderately affected their effectiveness at work. ** $P < 0.01$; *** $P < 0.001$ vs baseline.

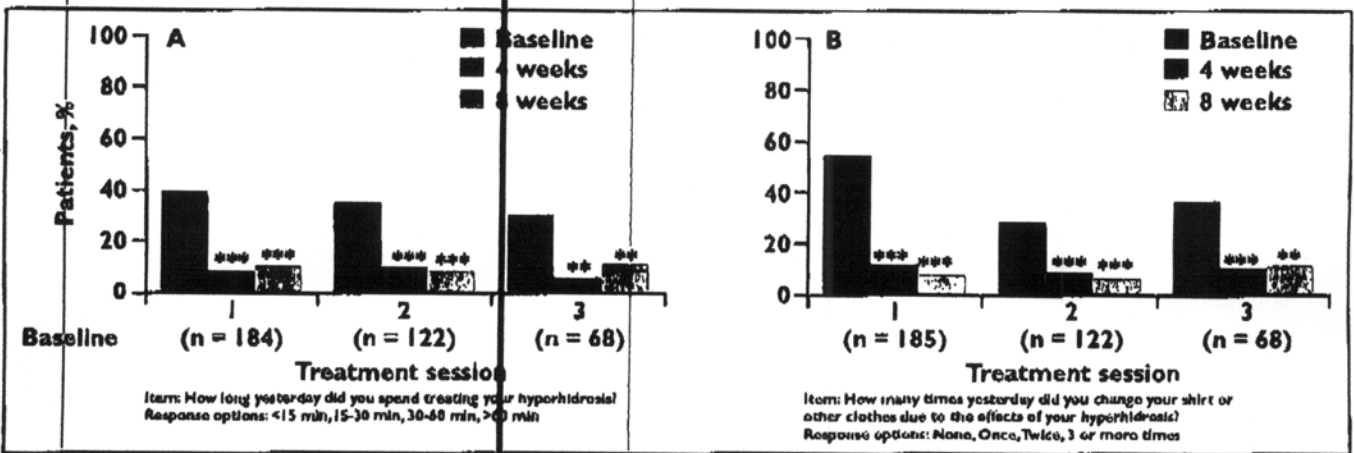


Figure 4. Time spent managing symptoms before and after treatment with BoNTA. (A) Patients who spent 15 minutes or more the previous day treating their hyperhidrosis; (B) Patients who changed their clothing at least twice the previous day because of hyperhidrosis. ** $P < 0.01$; *** $P < 0.001$ vs baseline.

2 or more times on the previous day before treatment, which decreased to 9%–12% at 4 weeks after treatment ($P < 0.001$) (Figure 4B)

Psychological impairment

- Significantly fewer patients reported feeling emotionally damaged or injured because of their hyperhidrosis after treatment than before treatment (Figure 5)
 - 76%–83% of patients felt emotionally damaged or injured because of their hyperhidrosis before treatment
 - 32%–42% of patients felt emotionally damaged or injured because of their hyperhidrosis at 4 weeks after treatment ($P < 0.001$)

Limitations in interpersonal and social situations

- Patients reported significantly less limitation in personal and social situations because of their hyperhidrosis after treatment than before treatment
 - 21%–35% of patients felt at least moderately limited on family occasions or with friends before treatment, which decreased to 2%–5% at 4 weeks after treatment ($P < 0.01$) (Figure 6A)

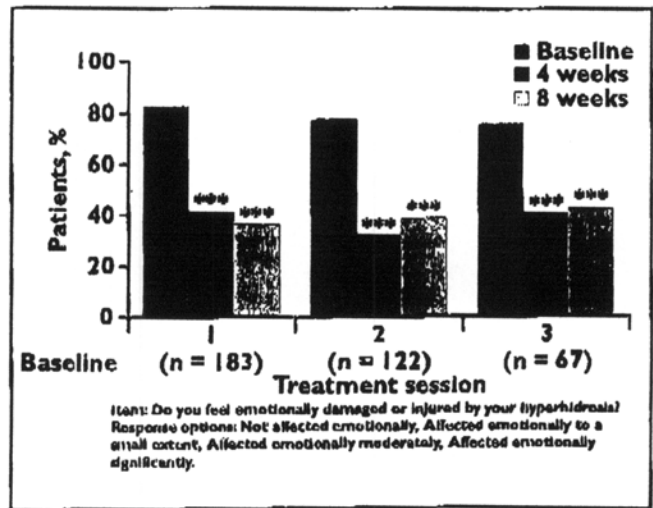


Figure 5. Psychological impairment before and after treatment with BoNTA. Patients who felt emotionally damaged or injured, at least to a small extent, because of their hyperhidrosis. *** $P < 0.001$ vs baseline.

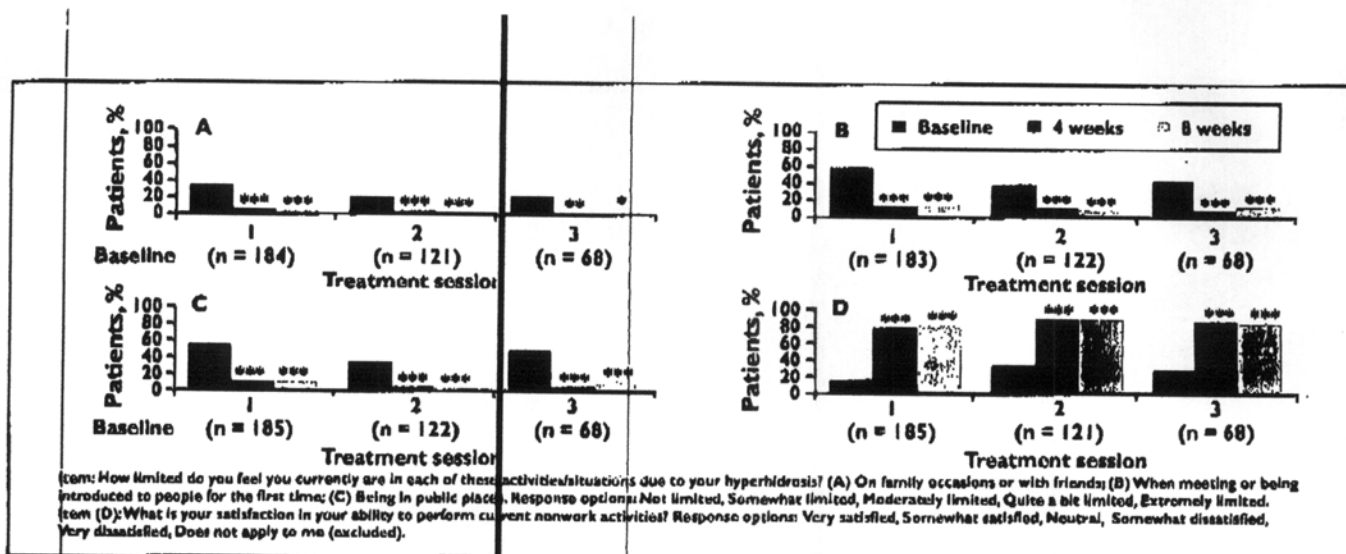


Figure 6. Limitations in interpersonal and social situations before and after treatment with BoNTA. (A) Patients who felt at least moderately limited at family occasions or with friends because of hyperhidrosis; (B) Patients who felt at least moderately limited when meeting or being introduced to new people because of hyperhidrosis; (C) Patients who felt at least moderately limited in public places because of hyperhidrosis; (D) Patients who were somewhat or very satisfied with their ability to perform nonwork (social and leisure) activities. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ vs baseline.

- 39%–58% of patients felt at least moderately limited in meeting new people before treatment, which decreased to 8%–14% at 4 weeks after treatment ($P < 0.001$) (Figure 6B)
- 35%–55% of patients felt at least moderately limited in public places before treatment, which decreased to 5%–11% at 4 weeks after treatment ($P < 0.001$) (Figure 6C)
- 17%–33% of patients were somewhat or very satisfied with their ability to perform nonwork activities before treatment, which increased to 78%–88% at 4 weeks after treatment ($P < 0.001$) (Figure 6D)

SUMMARY

- Patients with primary axillary hyperhidrosis have substantially reduced HRQOL because of their condition. Treatment with BoNTA improved HRQOL and limitations in daily activities in these patients
- As the effect of BoNTA waned and symptoms returned, impaired HRQOL and daily activities limitations recurred in parallel. However, repeated treatment with BoNTA after the recurrence of symptoms produced consistent and reproducible benefit in terms of improved HRQOL and daily functioning

CONCLUSIONS

The data reported here show that repeated treatment with BoNTA over 2 years is effective and consistently results in meaningful improvements in HRQOL and occupational, psychological, and personal functioning in patients with severe persistent primary axillary hyperhidrosis.

Disclosures

Dr. Glaser is an investigator for and consultant to Allergan, Inc. Dr. Kowalski, Dr. Weng, Ms. Ravelo, Mr. Daggert, Ms. Nordquist, and Ms. Emilio are employees of Allergan, Inc.

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Notes

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.