EFFECT OF BOTULINUM TOXIN TYPE A TREATMENT FOR SEVERE PRIMARY AXILLARY HYPERHIDROSIS ON WORK PERFORMANCE AND PRODUCTIVITY: RESULTS FROM AN OPEN-LABEL CLINICAL STUDY

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INTRODUCTION

Primary focal hyperhidrosis is a chronic, idiopathic condition characterized by excessive sweat production beyond physiologic need, and typically involves the underarms (axilla), the palms, the soles of the feet, or the face.[1] Primary axillary hyperhidrosis (PAH) can substantially impair the occupational, emotional, and physical status of affected individuals.[2-5] It is estimated that as many as 0.5% of the U.S. population (1.3 million persons) suffers from axillary sweating that frequently or always interferes with their daily activities.[6]

Presenteeism, the decline in on-the-job productivity resulting from worker illness, is a significant yet hidden cost to employers.[7] It is estimated that presenteeism accounts for 18% to 60% of all health-related expenses for companies in the United States.[8] Presenteeism has been associated with chronic medical conditions ranging from allergies to osteoarthritis, which result in quantifiable reductions in on-the-job functioning.[9-12]

Current data suggest that hyperhidrosis negatively affects patient work performance and productivity as indicated by responses to work-specific items in the Dermatology Life Quality Index (DLQI) and the Hyperhidrosis Impact Questionnaire (HHIQ).[3,4,13]. As part of an open-label safety study on botulinum toxin type A (BoNTA) treatment of PAH, the Work Limitations Questionnaire (WLQ) was incorporated to measure the extent to which PAH affects presenteeism.[14] Full-time employees with severe PAH were limited in performing physically demanding tasks 25% of the time, in mental and interpersonal tasks 20% of the time, in time management 17% of the time, and in work output 11% of the time.[14]

From the same open-label study of BoNTA treatment of PAH, we present the level of work performance and productivity limitations employees with PAH experience 30 days post-BoNTA treatment.

OBJECTIVES

- To describe the effect of BoNTA treatment of PAH on work performance and productivity by comparing mean Day 30 WLQ scale and Index scores to those at baseline for all full-time employed patients with PAH of any severity and for those patients with severe PAH
- To benchmark the Day 30 post-BoNTA treatment WLQ scale and Index scores reported by patients with severe PAH with:
  - Healthy control subjects
  - Patients who have chronic conditions such as osteoarthritis, depression, or rheumatoid arthritis
  - Responses from the general population on the assessment of their overall health status

METHODS

Study Population

- Patients enrolled in an open-label clinical study at sites in the U.S. who were 18 years or older, and had a clinical diagnosis of persistent PAH that interfered with daily activities and was resistant to topical treatment.
  - Patients received 50U/axilla of BoNTA (manufactured by Allergan, Inc., Irvine, CA)
  - Exclusion criteria included a clinical diagnosis of secondary hyperhidrosis, the presence of uncontrolled systemic disease, and concurrent use of any hyperhidrosis treatments other than over-the-counter antiperspirants or deodorant.
  - Data from patients who indicated they worked full-time were selected for analysis
- Hyperhidrosis symptom severity was collected at baseline using the Hyperhidrosis Disease Severity Scale (HDSS). The HDSS is a validated and reliable 4-point scale with which the patient rates the tolerability of his or her underarm sweating and the degree of interference with daily activities.[15] (Table 1)
  - An HDSS score of 3 or 4 indicates severe disease that is at a minimum barely tolerable and frequently interferes with daily activities; an HDSS score of 1 or 2 represents a milder form of disease with a lesser degree of impairment in daily activities

TABLE 1: HYPERHIDROSIS DISEASE SEVERITY SCALE (HDSS)

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

Work Limitations Questionnaire (WLQ)

- The WLQ is a valid and reliable 25-item instrument that measures employees experiences of work limitations and productivity losses due to their health problems[16]
- Patients rate their ability to perform tasks on 4 work limitation scales: Time Management, Physical Demands, Mental and Interpersonal Demands, and Output Demands (Table 2)
  - Responses for each are summed and reported as a scaled score of 0 (limited none of the time) to 100 (limited all the time)
  - Transformed scale scores indicate the percentage of time that patients were limited in performing a specific dimension of work in the prior two weeks and as such estimates health-related deficits in work performance
- The WLQ Index is the weighted sum of the scores from the 4 WLQ scales and estimates overall health-related productivity loss

Benchmark Populations

- WLQ data from several different populations were drawn from a database maintained by the developer of the WLQ (Debra Lerner, Ph.D.) and were matched by age, race, and gender to patients with severe PAH. This database includes WLQ scores from patients with a medical condition and from healthy subjects.
- Healthy controls
  - Subjects were screened by their primary care physician and had no major chronic conditions. The sample (752 observations) includes repeat measures of patients
- Patients with osteoarthritis
  - Patients (n = 230) were diagnosed with osteoarthritis by a physician
- Patients with depression
  - Patients were screened for depression by a primary care physician. Data from patients meeting DSM-IV criteria for major depressive disorder in the past two weeks, dysthymia, or both (double depression) were included. The sample (944 observations) includes up to 4 repeat measures per patient

- Patients with rheumatoid arthritis
  - Patients were diagnosed with rheumatoid arthritis by a primary care physician or a rheumatologist. The sample (404 observations) includes repeat measures of patients
- Patient responses on their overall health status
  - Patients were part of the National Survey of Work and Health, and are a nationally representative sample of adults in U.S. households. WLQ scores stratified by patients' perception of their general health as poor (n = 112), good (n= 350), very good (n = 378), and excellent (n = 359) are reported here.

Statistical analyses

- Two-tailed paired t tests were used to evaluate differences between Day 30 and baseline in the four WLQ scale scores and WLQ Index scores
  - A P value of ≤ 0.05 was considered statistically significant
- Data from patients with hyperhidrosis and from comparator groups were not compared through statistical analysis because the data collection methods varied among the groups

TABLE 2: WORK LIMITATIONS QUESTIONNAIRE (WLQ) SCALES

Scale	Assessment	Number of items	Range of scores
Physical Demands	Measures a person's ability to perform job tasks that involve body strength, movement, endurance, coordination, and flexibility (eg, move from place to place, carry items, stay in one position for more than 15 minutes, use handheld equipment)	6	0–100
Mental-Interpersonal Demands	Measures difficulties in performing cognitive job tasks and tasks that involve the processing of sensory information (eg, ability to keep mind on work, work carefully, speak with people in-person)	9	0–100
Time Management	Measures difficulties in meeting a job's time and scheduling demands (eg, work the required number of hours, work without stopping to take breaks, stick to a routine)	5	0–100
Output Demands	Measures a person's ability to meet demands for quantity, quality, and timeliness of work (eg, ability to handle workload, do work without making mistakes, finish work on time)	5	0–100

RESULTS

Of 158 patients enrolled in the study, there were 90 patients with PAH who were working full-time at baseline

- At baseline, 44 patients reported milder PAH (HDSS scores of 1 or 2) and 46 reported severe PAH (HDSS scores of 3 or 4) (Table 3).
- The mean age was 32. 60% were male and 82% were white.
- Patients with severe primary axillary hyperhidrosis (HDSS 3 or 4) at baseline reported statistically significantly greater mean Physical Demands and Time Management scale scores than patients with milder disease (P = 0.0226 and 0.0425, respectively) (Figure 1)
- Patients with severe primary axillary hyperhidrosis also reported greater mean baseline scores on the Mental-Interpersonal and Output Demands scales but the differences between these scores and those of patients with milder disease were not statistically significant (P = 0.094 and 0.834, respectively). (Figure 1)

TABLE 3: PATIENT DEMOGRAPHICS

Patient characteristics	All patients (n = 90)	Patients with HDSS scores 1 or 2 (n = 44)	Patients with HDSS scores 3 or 4 (n = 46)
Mean age (range)	32 (20-54)	34 (20-54)	30 (20-52)
Males, n %	54 (60%)	28 (64%)	26 (57%)
Ethnicity, n %			
White	74 (82%)	36 (82%)	38 (83%)
Black	4 (4%)	2 (5%)	2 (4%)
Asian	2 (2%)	1 (2%)	1 (2%)
Hispanic	7 (8%)	4 (9%)	3 (7%)
Other	3 (3%)	1 (2%)	2 (4%)

Improvement in work performance and productivity at Day 30 post-BoNTA treatment:

Patients with PAH

Patients with PAH reported substantial and statistically significant improvements in their work performance and productivity at Day 30 post-BoNTA treatment compared to baseline, as indicated by their mean WLQ scale and index scores (Figure 2).

- At baseline prior to treatment, patients with PAH reported that they were limited in time management 14.1% of the time, in physically demanding tasks 18.5% of the time, in mental and interpersonal tasks 16.8% of the time, and in work outputs 10.4% of the time.
- At Day 30 post-BoNTA treatment, statistically significant improvements were reported in all mean WLQ scale scores. Limitations were reduced to:
  - 4.8% of the time in time management (P <0.0001)
  - 8.2% of the time in physically demanding tasks (P = 0.01)
  - 7.2% of the time in mental and interpersonal demands (P <0.0001)
  - 5.1% of the time in work outputs (P = 0.0143)
- Overall work productivity was statistically significantly improved in patients with PAH at Day 30 compared to baseline, as indicated by a 4% loss in work productivity at baseline to 1.8% loss at Day 30 post-BoNTA treatment (P < 0.0001).

Patients with Severe PAH

- As previously presented, patients with severe PAH reported substantial health-deficits in work performance and productivity at baseline prior to treatment.[14] Patients with severe PAH were limited in time management 17.6% of the time, in physically demanding tasks 25.2% of the time, in mental and interpersonal tasks 20.0% of the time, and in work output 10.9% of the time. [14]
- At Day 30 post-BoNTA treatment, statistically significant improvements were reported in time management and in mental and interpersonal tasks, with limitations reduced to 6.1% and 8.0% of the time, respectively (P = 0.0005 and P = 0.001, respectively) (Figure 3)
- Patients with severe PAH also reported lower mean scores at Day 30 on the Physical Demands and Output Demands scale, but these scores were not statistically significantly different from those at baseline (P = 0.0618 and 0.0906, respectively).
- Overall work productivity, as measured by the WLQ Index score, was statistically significantly improved in patients with severe PAH at Day 30 post-BoNTA treatment compared to baseline (P = 0.0017).
- A 3% improvement in overall work productivity was observed at Day 30 compared to baseline.

Benchmarking the effect BoNTA treatment of severe PAH on work performance productivity

- At baseline prior to treatment, patients with severe PAH reported a substantial reduction in work performance in all work domains compared with patients from an age-, race-, and gender-matched sample of healthy controls.[14]
- Patients with severe PAH reported levels of work performance impairment that was similar to those reported by patients with osteoarthritis, depression, rheumatoid arthritis, and individuals who perceived their general health as poor.[14] Overall work productivity loss, as measured by the WLQ Index, was comparable to the population who perceived their health as Poor. Overall work productivity loss due to severe PAH was estimated at 4.9% [14].
- At Day 30 post-BoNTA treatment, patients with severe PAH reported work performance (in the Time Management, Mental and Interpersonal Demands, and Output Demands scales) that was similar to those reported by healthy controls, and substantially lower than those reported by patients with chronic diseases such as osteoarthritis, depression, or rheumatoid arthritis (Figures 4A – 4D).
- At Day 30 post-BoNTA treatment, the work performance of patients with severe PAH had improved to levels that were similar to those reported by individuals who perceived their general health status to be in the range of good to excellent (Figures 4A – 4D).
    - Mean Time Management and Output Demands scale scores were improved to levels that were similar to those of individuals who rated their general health as excellent (Figures 4A and 4D).
    - Mean Physical Demands scale score at was improved to a level that was most similar to that of the population who perceived their general health as good (Figure 4B).
    - Mean Mental and Interpersonal Demands scale score at was improved to a level that was most similar to that of the population who perceived their general health as very good (Figure 4C).
- At Day 30 post-BoNTA treatment, the overall work productivity loss for patients with severe PAH was reduced to approximately 2%. This is comparable to the overall work productivity loss expressed by the general population who perceived their health as Excellent (1.8% loss in work productivity).

Figure 1: Mean baseline WLQ scale scores for patients with primary axillary hyperhidrosis with HDSS scores of 3 or 4 (n = 46) versus patients with HDSS scores of 1 or 2 (n = 44).
(TM) Time Management scale; (PD) Physical Demands scale; (MI) Mental-Interpersonal Demands scale; (OD) Output Demands scale; (Index) WLQ Index score.

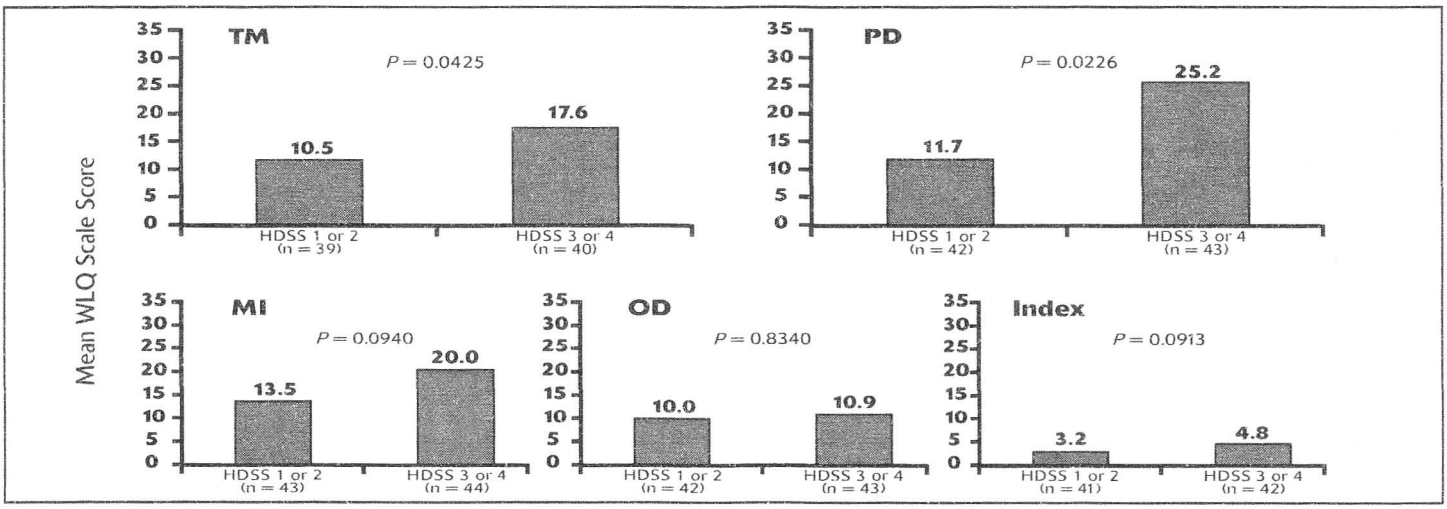


Figure 2: Mean WLQ scale and Index scores at baseline and Day 30 post-BoNTA treatment for all full-time employed patients regardless of their HDSS scores.
(TM) Time Management scale; (PD) Physical Demands scale; (MI) Mental-Interpersonal Demands scale; (OD) Output Demands scale; (Index) WLQ Index score.

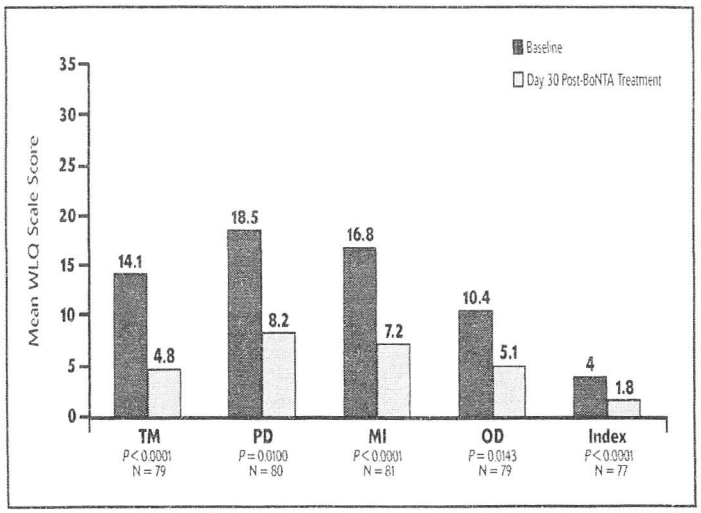
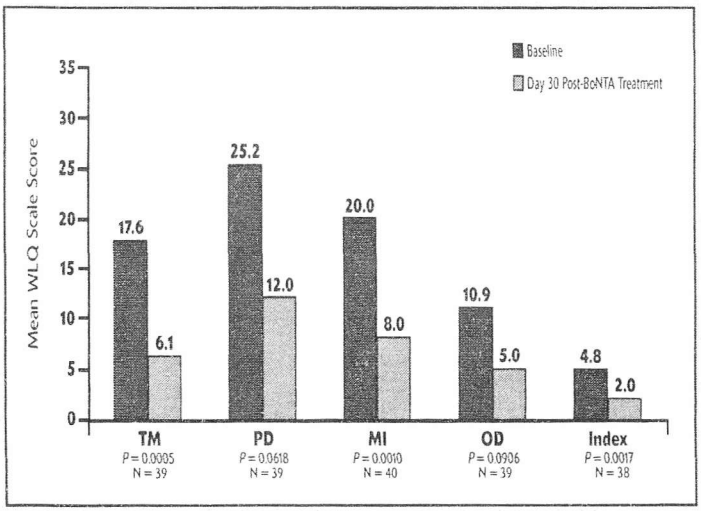
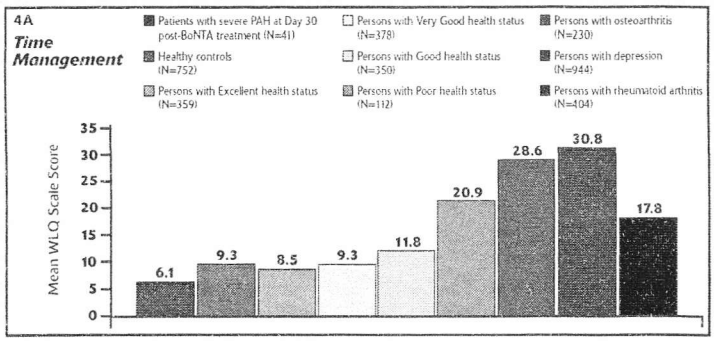
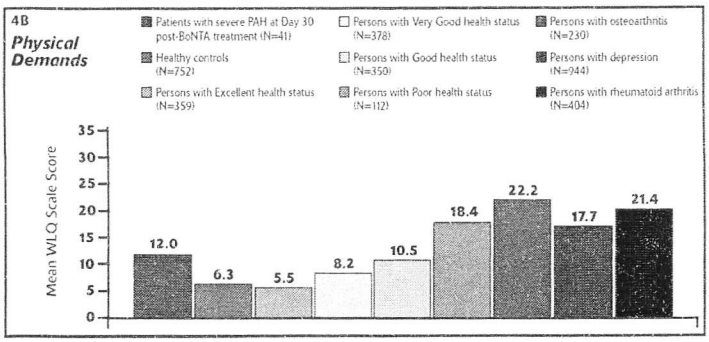


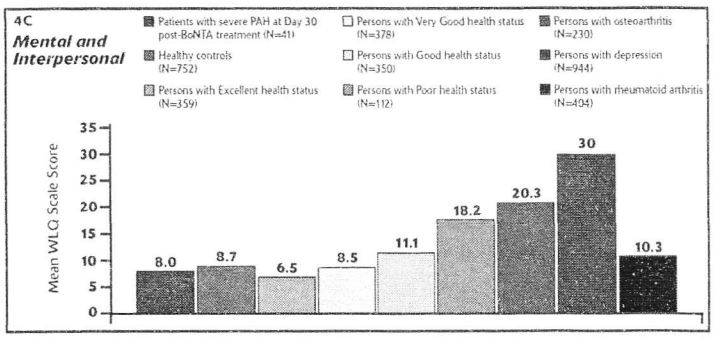
Figure 3: Mean WLQ scale and Index scores at baseline and Day 30 post-BoNTA treatment for full-time employed patients who indicated having severe primary axillary hyperhidrosis at baseline (i.e., HDSS score of 3 or 4).
(TM) Time Management scale; (PD) Physical Demands scale; (MI) Mental-Interpersonal Demands scale; (OD) Output Demands scale; (Index) WLQ Index score.

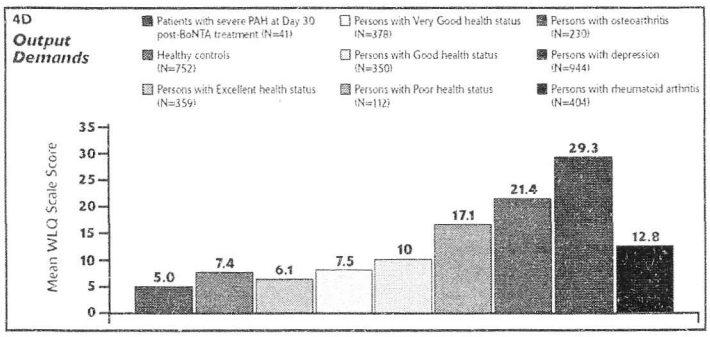


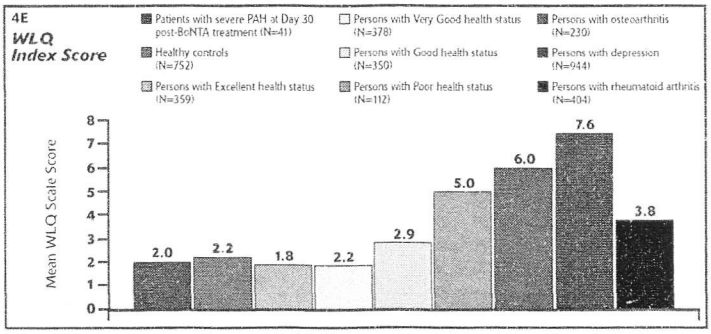
Figures 4A-4E: Benchmarking of mean WLQ scale scores for patients with severe primary axillary hyperhidrosis (HDSS scores of 3 or 4) at day 30 post-BoNTA treatment compared to available WLQ data from age-, race-, gender-matched patient samples. (4A) Time Management scale; (4B) Physical Demands scale; (4C) Mental-Interpersonal Demands scale; (4D) Output Demands scale; (4E) WLQ Index score.











CONCLUSIONS

BoNTA treatment of severe primary axillary hyperhidrosis results in quantifiable and meaningful improvements in work performance and productivity, particularly in the areas of time management and mental and interpersonal demands, as measured by statistically significant reductions in these WLQ scale scores at Day 30 post-treatment. Thirty days post-treatment, patients with severe PAH reported that their ability to perform work-related tasks requiring time management and mental and interpersonal demands had improved to levels that were similar to those reported by healthy controls and individuals who rated their general health status as good, very good, or excellent.

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Note: Dosing and results reported in this study are specific to the formulation of botulinum toxin type A manufactured by Allergan, Inc. (Irvine, CA). 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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