Australasian Journal of Dermatology

Australasian Journal of Dermatology (2011) **52**, 123–126 doi: 10.1111/j.1440-0960.2010.00723.x

CASE REPORT

Thirty-five units of botulinum toxin type A for treatment of axillary hyperhidrosis in female patients

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ABSTRACT

We present a retrospective audit on efficacy and impact of 35 units of botulinum toxin type A per axilla on quality of life in female patients with axillary hyperhidrosis. This audit shows that 35 units of botulinum toxin type A is a reasonable starting dose and could significantly improve patients' quality of life and reduce the cost of treatment.

Key words: axillary hyperhidrosis, botulinum toxin, QOL, quality of life.

INTRODUCTION

Primary axillary hyperhidrosis is a chronic condition that is characterized by the presence of excessive sweating in the axillary region for a duration greater than 6 months, with at least two of the following features: bilateral sweating; positive family history; age of onset under 25; minimum occurrence once per week; does not occur when the patient is asleep.[1] It is known to significantly affect quality of life (QOL), impacting on functional, social, personal, emotional and professional domains. An estimated 1.4% of the US population has axillary hyperhidrosis and 0.5% suffers debilitating symptoms that interfere with daily activities.[2]

Treatment options currently available to patients with primary axillary hyperhidrosis can be categorized as non-surgical or surgical. Non-surgical options are often limited by poor tolerability and short-lived effect.[3] Surgical approaches often carry a high risk of potentially serious side effects with approximately 20% of patients dissatisfied with treatment outcomes.[4] Botulinum toxin injection is minimally invasive and has become a therapy of choice for patients who fail to respond to more conservative treatment prior to, or instead of, resorting to surgery.

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Submitted 3 June 2008; accepted 18 October 2009.

Acetylcholine is the main neurotransmitter that innervates the eccrine sweat glands. Botulinum toxin type A (BonTA) is a powerful acetylcholine inhibitor. Small amounts injected into or near muscles or sweat glands can cause a localized, long-lasting but reversible decrease in cholinergic transmission.

A 52-week randomized study of two different concentrations of BonTA found that 50 units (U) had no significant difference in treatment efficacy (including duration of symptom-free intervals) or improvement in QOL compared to 75 U.[5] Thus 50 U became the current standard practise for the starting dose. We have therefore undertaken a retrospective audit regarding the efficacy (achieving 50% or more improvement in a gravimetric sweat test four weeks after the initial treatment) and impact on QOL of 35 U of BonTA per axilla in female patients with axillary hyperhidrosis.

METHODS

Patients

Between December 2005 and August 2009 there were 30 female patients who presented to our institution with bilateral axillary hyperhidrosis. Patients were screened for systemic diseases that cause hyperhidrosis, neuromuscular diseases and for a history of use of BonTA in the past year. Pregnant and lactating women were excluded from treatment with BonTA

Study design

All patients received 35 U of BonTA/axilla. An additional 15 U of BonTA was permitted at their week 4 assessment based either on their subjective satisfaction, QOL result or gravimetric sweat result.

Abbreviations:

QOL	Quality Of Life
BonTA	Botulinum Toxin type A
U	units
HDSS	Hyperhidrosis Diseases Severity Scale
DLQI	Dermatology Life Quality Index

Previous treatment, medical history, family history of hyperhidrosis, result of gravimetric sweat test, QOL and follow-up results were entered into the hyperhidrosis data registry at the time of treatment.

The objective quantification of the sweat test and a QOL questionnaire were performed immediately prior to injection and again four weeks after treatment.

The QOL questionnaire measured 26 indices and assessed the impact of hyperhidrosis on various aspects of the patients' life (e.g. daily activities, career, health, psychosocial issues and subjective improvement following treatment). The result had five levels, ranging from 26 (no effect) to 130 (extreme impact).

Gravimetric sweat test

A 150 mm-diameter round filter paper (Whatman International Ltd, Maidstone, England) was weighed on high precision laboratory scales (Sartorius CP224S, Sartorius AG, Gottingen Germany) and the weight recorded. The paper was then placed under the axilla for 5 min and reweighed. The difference between the two weights was taken as sweat production in milligrams over 5 min. Only data of patients who had a baseline gravimetric measurement of spontaneous resting sweat production of at least 50 mg/axilla/5 min were used in the study.[6] The vial of BonTA (100 U, Botox, Allergan Inc, Irvine, CA, USA) was reconstituted with 5 ml of 0.9% bacteriostatic sodium chloride. The area was identified by blotting paper. The axilla was injected intradermally, 1.5–2.0 cm apart.

Patients were assessed four weeks after the BonTA injections. Patients who were satisfied with treatment and unable to attend follow up received a telephone call to fill in the post-treatment QOL questionnaire. Subjective opinion regarding benefit allowed patients to have re-treatment of 15 U/axilla, despite achieving at least 50% sweat reduction of their baseline value. Thus, for clarity, the patients were divided into groups based on their week 4 responses: responder and non-responder. This paper illustrates the three ways of categorizing this: (i) objectively by gravimetric sweat test measurement (achieving primary efficacy); (ii) subjectively by QOL score; or (iii) individual's satisfaction.

RESULTS

To qualify for the study subjects had to produce a minimum of 50 mg/5 min of sweat. Of the 30 prospective subjects 16 patients qualified. Fourteen patients were not included in this study due to incomplete assessments.

Gravimetric sweat test measurement

Of the 12 patients who completed the pre- and post-treatment gravimetric measurement, 75% (9/12) of responders experienced a 50% or greater reduction in sweating, while 42% (5/12) had achieved ≥ 90% sweat reduction. The mean gravimetric measurement of sweat reduction comparing those who were satisfied with treatment (253 mg/5 min) versus those requiring additional injection (326 mg/5 min) was statistically significant at $P < 0.05$. (Fig. 1)

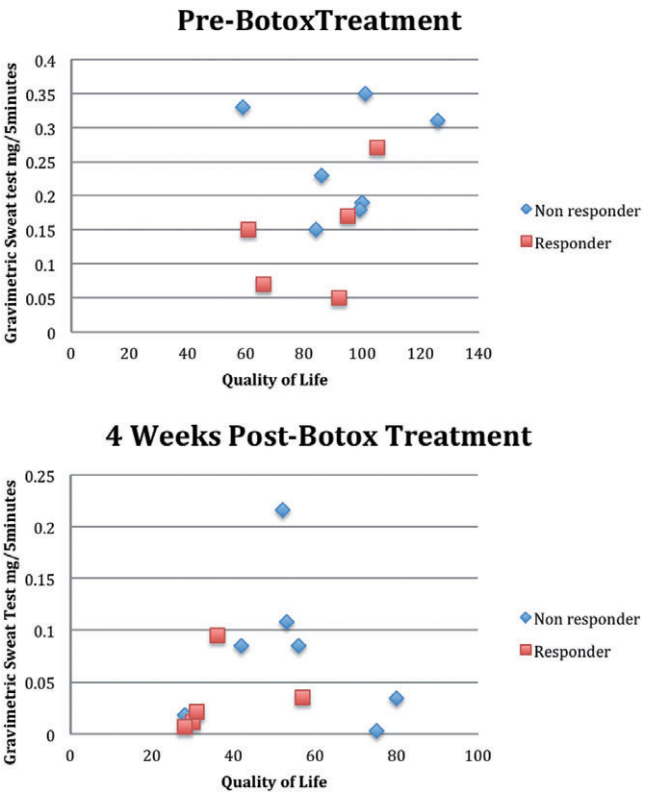

Figure 1 Correlation between quality of life and gravimetric sweat test before and after 35 units of botulinum toxin type A treatment.

The remaining four patients were followed-up by telephone consultation and showed significant improvement in their QOL. Prior to treatment they subjectively considered that they had moderate to severe hyperhidrosis which, after treatment, was reduced to mild. (Fig. 2)

Quality of life outcome

All 16 patients completed pre- and post-treatment QOL surveys. Prior to treatment two (12%) patients felt their axillary hyperhidrosis had a slight effect on their QOL while six (38%) reported a moderate effect, seven (44%) reported a severe effect and one (6%) reported an extreme effect on daily activity.

The post-treatment QOL survey showed an overall reduction in effect on QOL; six (38%) patients had little or no effect from hyperhidrosis, eight (50%) reported a slight effect and only two (12%) felt that their hyperhidrosis had a moderate effect on their daily life. However there is no significant difference in QOL pre- and post-treatment with 35 U of BonTA between both groups ($P = 0.07$). (Table 1)

Comparing the two different groups depending on their satisfaction, mean QOL total score at study baseline were significantly higher in group 2 (93.7 +/– 20.5) than group 1

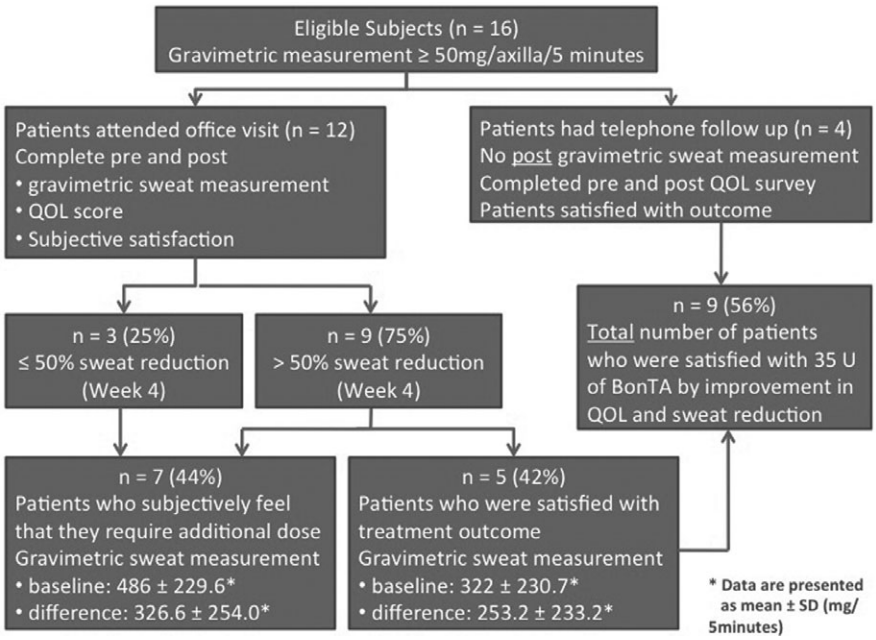

Figure 2 Patients' treatment outcome. BonTA, botulinum toxin type A; QOL, quality of life.

Table 1 Comparison of patients' quality of life (QOL) scores pre and post 35 U botulinum toxin type A

		Satisfied ($n = 9$)		Required additional Rx ($n = 7$)		Total ($n = 16$)	
QOL score	Level of effect	Pretreatment	Post-treatment	Pretreatment	Post- treatment	Pretreatment	Post- treatment
26–39	1	0%	55.5%	0%	14.3%	0%	38%
40–65	2	11.1%	44.4%	14.3%	57.1%	12%	50%
66–91	3	44.4%	0%	28.6%	28.6%	38%	12%
92–117	4	44.4%	0%	42.9%	0%	44%	0%
118–130	5	0%	0%	14.3%	0%	6%	0%

(84.1 +/– 18.1). Despite achieving at least 50% sweat reduction, group 2 still had a higher post-treatment mean QOL total score than group 1, 55.2 +/– 17.9 versus 38.8 +/– 11.4. Although both groups had a statistically significant ($P < 0.001$) change in mean reduction of the QOL score, 45.3 +/– 19.6 and 38.5 +/– 22.4, there is no significant difference between the two groups ($P = 0.07$). (Fig. 3)

Satisfaction result

Of the 16 patients, 12 attended post-treatment follow up and were categorized into two groups. Group 1 was patients who were satisfied with treatment. Group 2 were patients who were dissatisfied with treatment. Group 1 consisted of five (42%) patients who felt that they had significant benefit and achieved at least 50% sweat reduction by the gravimetric sweat test at four week follow up. Combined with the four patients who were followed up by phone consultation, this brought the number of patients who were satisfied with 35 U of BonTA/axilla to a total of nine. Thus, out of the 16 patients, 56% (9/16) were satisfied with their result first time. Group 2 consisted of seven (44%) patients who felt

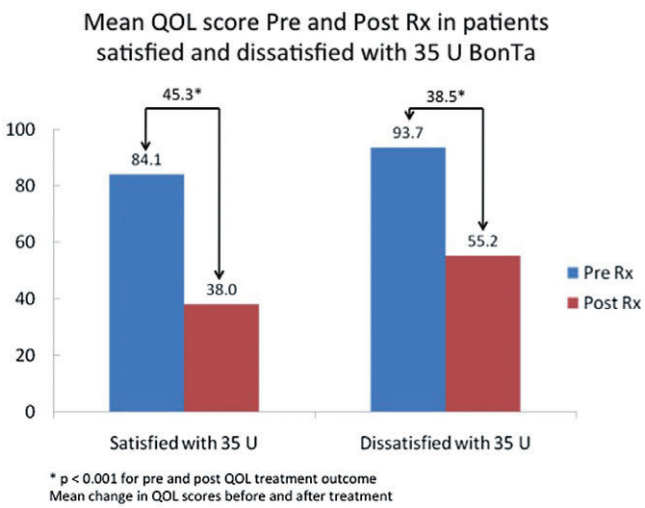

Figure 3 Mean quality of life (QOL) score before and after treatment with 35 U of botulinum toxin type A (BonTA).

that they had not achieved a significant benefit from 35 U, despite four of the patients achieving more than 50% sweat reduction.

DISCUSSION

BonTA is known to be one of the most effective treatment options for axillary hyperhidrosis. Most studies have been conducted using 50 U of BonTA per axilla in both male and female patients, aiming for greater than 50% sweat reduction and achieving at least a 2-point improvement in the Hyperhidrosis Diseases Severity Scale (HDSS) four weeks after treatment.[5]

Baseline characteristics in this study were similar to other studies. Instead of measuring HDSS and Dermatology Life Quality Index, our centre used our own specific hyperhidrosis QOL questionnaire.

The result of this audit process has provided an opportunity to assess the benefit of 35 U of BonTA in female patients with axillary hyperhidrosis. Our results showed that 75% of surveyed patients had reached the primary efficacy endpoint – achievement of more than 50% sweat reduction four weeks after treatment. Although there is no placebo comparison used in this study, other literature has shown that placebo has a much lower response rate of 33%.[1,5,7]

Subjectively, 55% of patients had significant improvement in their QOL to the point that their hyperhidrosis had little or no impact on them.

The patients that requested an additional 15 U/axilla injection had higher pre- (486 ± 229.6 vs 322 ± 230.7 mg/5 min), and post-gravimetric measurements of sweat production. This suggests that the dose could be tailored to an objective measure of sweat load pretreatment.

In this group, four patients had achieved more than 50% sweat reduction, but higher QOL scores at four weeks follow up. Despite a 75% response rate, 56% were satisfied with the treatment. This gives a reflection of clinical practice where individual's satisfaction is likely to be the primary factor in the decision to retreat. This corresponds with other studies where timing of re-treatment should be determined subjectively by the patient based on their HDSS[5].

Further research is required to identify a suitable quantitative result correlating to 35 U of BonTA and whether this can achieve a similar duration of relief of symptoms as in other studies, (range 3–14 months).[5,7]

In conclusion, these preliminary findings show that female patients with idiopathic axillary hyperhidrosis who have lower gravimetric sweat test results could benefit from 35 U of BonTA as a reasonable starting dose which contributes significantly to improving patients' QOL as well as significantly reducing the cost of treatment.

ACKNOWLEDGEMENTS

We would like to thank Associate Prof Greg Goodman who contributed the initial study concept of creating and setting up the Hyperhidrosis Data Registry and creating the hyperhidrosis QOL questionnaire, the nurses for administering the study protocols and Marlene Rennie, who provided data entry, Simon Cumming who designed the registry and undertook the statistical calculation of the data with SPSS 18 (SPSS Inc., Chicago, IL, USA). Variables were measured with parametric (independent sample *t*-test and paired sample *t*-test).

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