Patient satisfaction after the treatment of glabellar lines with Botulinum toxin type A (Speywood Unit): a multi-centre European observational study

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Abstract

Background Whilst the efficacy and safety of glabella complex treatment with botulinum toxin type A (Speywood Unit) [BoNT-A (s.U)] has been comprehensively studied, there are very few trials on patient-reported outcomes and patient satisfaction associated with this treatment.

Objective To assess the level of patient satisfaction 3 weeks and 4 months after the treatment of glabellar lines with BoNT-A (s.U).

Methods This is a multi-centre, prospective, non-interventional observational study carried out in France, Germany, Spain and the United Kingdom. Subjects were eligible if the investigator had already decided to prescribe BoNT-A (s.U), according to the labelling. Subjects completed a questionnaire at both 3 weeks and 4 months after treatment.

Results About 533 subjects completed at least one of the two questionnaires. About half of the subjects (47.9%) were naive to BoNT-A treatment of the glabella, while 50.6% had previously received another product. A high level of satisfaction was observed after the treatment, with 94.7% and 89.6% of subjects being satisfied or very satisfied with the aesthetic outcome at week 3 and month 4, respectively. Treatment was safe and well tolerated, as directly determined in the survey. Major reasons for satisfaction included the positive aesthetic outcome, a natural appearance, a rested look and comfort of injection. Most subjects felt the treatment brought them ‘harmony’, ‘self-esteem/confidence’ or ‘youth’. Of the subjects who had previously been treated with another product, 51.2% considered the results obtained in the present study with BoNT-A (s.U) were better.

Conclusion Treatment of the glabellar lines with BoNT-A (s.U) led to a high level of patient satisfaction and a more positive self-perception up to 4 months after the treatment, regardless of whether the patients were naive or not to BoNT-A treatment.

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Conflicts of interest
All investigators received fees for conducting the study. Ms. Paliargues was a previous employee and Mr. Kerrouche is an employee of Galderma R&D. Patients received no payments for their treatments.

Introduction

Hyperfunctional wrinkles, such as the glabellar lines, are caused by repeated contraction of the facial muscles and can be effectively treated with muscle relaxants such as botulinum toxin type A (BoNT-A) blocking the release of the neurotransmitter acetylcholine, a key messenger for muscle contractions.1,2 Azuline3 is a BoNT-A quantified in Speywood Unit (s.U) [BoNT-A (s.U)]3, approved in Europe for the temporary improvement in appearance of moderate to severe glabellar lines seen at frown when severity of these lines has an important psychological impact on the patients. BoNT-A (s.U) is approved in the United States, Canada and other countries throughout the world as

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Dysport® (AbobotulinumtoxinA, Ipsen Pharma, Boulogne-Billancourt, France).

The efficacy and safety of BoNT-A (s.U) in the treatment of glabellar lines has been demonstrated in several randomized, double-blind, controlled trials.1–9 The average onset of action was 2–4 days after treatment (35% of patients had results by Day 2),10 and the duration of effect was at least 4 months, with efficacy maintained for up to 5 months.3,11 Outcomes were also reported to be highly consistent after repeated treatment cycles, with no loss of efficacy or tachyphylaxis (loss of previously noted effect).10,12 However, evaluation of psychological aspects such as patient perception have been limited to the evaluation of patient satisfaction. In a retrospective multi-country study of repeated BoNT-A (s.U) treatments in the upper face involving 945 patients, both physicians and subjects confirmed the high level of efficacy and safety over all treatment cycles: the median interval between 5 consecutive cycles was approximately 6 months.12 In a second study, Ascher and colleagues found that patient satisfaction was correlated with the efficacy of treatment, and that the majority of patients remained satisfied after 6 months.9

The objective of the present large-scale, multi-centre, prospective European observational study was to determine patient perception of a glabellar treatment with BoNT-A (s.U), including motivations for treatment, level of patient satisfaction after treatment and reasons for their satisfaction.

Materials and methods
This was a non-interventional, prospective study carried out at 66 centres in France, Germany, Spain and the United Kingdom. The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practices and was reviewed and approved by ethics committee when required by local regulations. Subjects did not receive compensation for participation in the study and all subjects completed written informed consent prior to enrolment. Participation did not influence the payment collected during the study.

Subjects were eligible if the investigator had already decided to prescribe BoNT-A (s.U) according to the labelling. Specifically, subjects were 18–64 years old, with moderate to severe glabellar lines at maximal frown and could be either naïve for BoNT-A or might have been treated previously with another BoNT-A product in the same area. BoNT-A (s.U) was prescribed and used with the usual standard of care and the treatment was at the discretion of the investigator and the subject.

Two different satisfaction questionnaires were used in the study, reflecting the different topics to be addressed at each time point (3 weeks and 4 months after the baseline injection). The week 3 questionnaire focused on the results after treatment and contained 14 single-choice questions and 1 multiple-choice question. The month 4 questionnaire focused on the duration of the treatment and contained 7 single-choice questions. Details of the questions asked at each time point and their respective possible answers are given in Table 1. For each single-choice question, at least one negative response was provided, enabling the subjects to give negative feedback regarding the treatment if they wished. Questionnaires were sent directly by the subjects to the data management team in a pre-paid envelope and were not handled by the injecting physician. Inclusion information, demographics of the subjects and adverse events were also collected during the study.

The population analysed included subjects who had completed at least one of the questionnaires. Subjects who did not complete either questionnaire were excluded from the final analyses. No inferential statistics were performed and all variables were summarized descriptively.

| Table 1 | Baseline characteristics (analysed population) |
|---------|-----------------------------------------------|
| Gender  |                                               |
|         | N   | Population analysed (%) |
| Male    | 51  | (9.7)                  |
| Female  | 474 | (90.3)                 |
| Severity of glabellar lines |       |
| N       | 525 |
| Moderate| 364 | (69.3)                 |
| Severe  | 161 | (30.7)                 |
| Perception of subject’s appearance |       |
| N       | 526 |
| Look younger | 245 | (46.6) |
| Look current age | 176 | (33.5) |
| Look older | 105 | (20.0) |
| Main reason for receiving injection |       |
| N       | 531 |
| Personal wish | 484 | (91.1) |
| Job requirement | 13  | (2.4)  |
| Pressure from spouse/friends/family | 19 | (3.6) |
| Other   | 15  | (2.8)                  |
| Top 3 reasons why BoNT-A (s.U) was prescribed (multiple choices possible) |       |
| N       | 526 |
| Experience with this product in other patients | 362 | (68.8) |
| Proven efficacy | 286 | (54.4) |
| Convenient product that allows patient satisfaction | 206 | (39.2) |

Results
A total of 559 subjects were enrolled in the study: 531 (95.0%) and 485 (86.8%) completed the satisfaction questionnaire at week 3 and month 4 respectively. The population analysed included 533 subjects who had completed at least one of the two questionnaires (531 subjects who had completed at least the first questionnaire and 2 new subjects who had completed only the second questionnaire). Only 26 subjects (4.7%) did not complete a questionnaire and were therefore excluded from the analysis.
Subject baseline characteristics
Baseline characteristics of the subjects enrolled in the study are included in Table 1. The mean age of subjects was 46.3 years (21–77 years), and the majority were female (90.3%). Approximately half of the subjects (252; 47.9%) had not previously received BoNT-A in the glabellar complex, while 266 subjects (50.6%) had previously received another BoNT-A product in their glabellar lines on average 12.7 months prior to enrollment in the present study. For the other BoNT-A product which some subjects received, the mean number of injection points was 5.3 and mean dose per point was 5.4 u (units as defined for the alternative product). At study baseline, more subjects presented with moderate glabellar lines (69.3%) and 20.0% perceived that they looked older than their age. The main reason for treatment was ‘personal wish (to enhance) appearance or attractiveness’ (91.1%), while other reasons were only cited in few cases. For the investigators, the main three reasons why BoNT-A (s.U) was prescribed included ‘experience with this product in other patients’ (68.8%), ‘proven efficacy’ (54.4%) and ‘convenient product that allows patient satisfaction’ (39.2%).

Injection details
On average, subjects were treated at baseline with a mean 5.3 points of injection and 10.6 s.U per point. Less than a quarter of subjects (112; 23.3%) received a subsequent minor (‘touch-up’) injection, the normal practice if subjects required fine adjustments after the initial treatment. There was considerable variability in the elapsed time after treatment when touch-ups were administered (20.9 ± 18 days). Each touch-up was, on average, 5.3 s.U per point in 2.5 points of injection. The requirement for touch-up injections was analysed in detail (Table 2).

Sub-group analyses were performed based on the gender of subject and the severity of wrinkles, two main aspects taken into consideration by the investigators at the time of treatment and which could influence the dose administered.

Gender
More male subjects had severe glabellar lines at baseline (62.7% male vs. 27.3% female) and were naive to BoNT-A (75.0% male vs. 40.6% female). Male subjects received a higher dose during the baseline injection (mean: 65.0 vs. 54.7 for females), as would be expected based on the different musculature (in particular, muscle mass and activity) of the male face. Correspondingly, more male subjects received a touch-up injection than female subjects (34.8% vs. 22.1%).

Severity at baseline
When compared to subjects with moderate glabellar lines at baseline, more severe subjects were male (19.9% vs. 5.2%), and naive to BoNT-A (50.0% vs. 42.9%). Severe subjects received higher doses at baseline injection (mean: 61.9 s.U vs. 52.9 s.U for moderate subjects). More severe subjects consistently received a touch-up injection than moderate subjects (28.8% vs. 21.0%).

Safety and tolerability of BoNT-A (s.U) injection
Treatment of glabellar lines with BoNT-A (s.U) was safe and well tolerated, with no injection site reactions or hypersensitivity observed in any subject in the study. The two most commonly reported adverse events included headache (6 subjects; 1.1%) and issues associated with the eyes (including ptosis, eyelid oedema, dry eye and twitching of muscles around the eyes – 2 subjects; 0.4%). When asked about the injection procedure, 92.4% of subjects were satisfied or very satisfied with the comfort of injection (Fig. 1a). Regarding the side-effects after injection, 76.2% of subjects were not bothered at all (Fig. 1b), a strong indication

Table 2 Analysis of touch-up injections provided to subjects

| Touch-up injection (n = 481) | Yes 112 (23.3%) | No 369 (76.7%) |
|------------------------------|-----------------|----------------|
| **IF YES:**                  |                 |                |
| Duration between 1st and 2nd injections in days (n = 111) | Mean ± SD 20.9 ± 18.0 (Min, max) (7, 133) | |
| Number of injection points (n = 112) | Mean ± SD 2.5 ± 1.1 (Min, max) (1, 6) | |
| Number of units per injection point (n = 112) | Mean ± SD 5.3 ± 3.4 (Min, max) (0, 20) | |
| Severity of glabellar lines at baseline (n = 112) | Moderate 70 (62.5%) | Severe 42 (37.5%) |

Figure 1 (a) Satisfaction with comfort and (b) subjects concerns about side effects of injection.
that treatment with BoNT-A is understood by many patients nowadays.

Subject’s satisfaction and self-perception after treatment

High levels of satisfaction were observed at both 3 weeks and 4 months after the treatment (Fig. 2). At week 3, 94.7% of subjects were satisfied or very satisfied with their aesthetic outcome in the glabellar complex and 93.4% of subjects found the results met or surpassed their expectations. At 4 months, 89.6% of subjects remained satisfied or very satisfied with the aesthetic outcomes and 88.7% of subjects found the results met or surpassed their expectations. Nearly all subjects reported that they would like to receive the treatment again (97.2% and 92.9% at week 3 and month 4, respectively) and would recommend it to their friends and family (96.2% and 93.4% at week 3 and month 4, respectively).

The levels of satisfaction were similarly high at week 3 and month 4 for the subjects who were both naive to BoNT-A and those who had previously received similar treatment. There was slightly less satisfaction at 3 weeks amongst subjects who received a touch-up injection than those who did not need one, as could be expected (90.9% vs. 95.6% of subjects satisfied or very satisfied with the aesthetic outcomes). However, both groups were similarly satisfied at month 4 (87.3% vs. 90.7%). At

Figure 2  Subject satisfaction regarding (a) aesthetic outcome, (b) the results in comparison with expectations and (c) post-treatment appearance.
both week 3 and month 4, a high level of satisfaction was observed regardless of the gender or the severity of glabellar lines at baseline.

The overall high level of satisfaction with treatment corresponded to a more positive self-perception after the treatment. Three weeks after the treatment, 82.0% of subjects said they appeared rested, 97.5% of subjects considered the result looked natural and 75.9% of subjects felt more attractive (Fig. 2c). While 20.0% of subjects felt they looked older than their age before any treatment was given, only 0.4% of subjects at week 3 and 0.8% of subjects at month 4 still thought so (Fig. 3a). Also, 78.9% and 74.8% of subjects felt they looked younger than their age at week 3 and month 4, respectively, compared to 46.6% at baseline (Fig. 3a). Similarly, 87.5% and 88.6% of subjects felt better about themselves 3 weeks and 4 months after the treatment, respectively (Fig. 3b). More specifically, subjects felt that the injection brought them more harmony (45.4% of subjects), self-esteem/confidence (44.3%) and/or youth (38.5%) (Fig. 4).

Comparisons with other products' treatments

Among subjects who had previously received injection of another BoNT-A product in the glabellar area, 51.2% considered the results obtained in the present study with BoNT-A (s.U) were better compared to 4.9% with another product; 43.9% considered them to be the same (Fig. 5a). For the duration of the

![Figure 3](image1.png)

Figure 3 Subject perception assessments prior and/or subsequent to the treatments regarding (a) age and (b) how subjects felt about themselves.

![Figure 4](image2.png)

Figure 4 Question: The treatment leads to more...? (more than one answer possible).
effects, 43.6% thought the results with BoNT-A (s.U) lasted longer, 9% thought the previous results lasted longer and 47.4% thought the duration was the same (Fig. 5b).

Discussion

The results of this large-scale European observational study showed that the most frequent reason for undergoing glabellar line injections was personal wishes (91.1%), rather than job requirements or pressure from spouse/friends/family. In her book on 'Living with your Looks', the psychologist R Honigman indicated that, when an individual makes a personal decision based on a desire to improve his or her confidence and self-esteem by altering appearance through cosmetic procedures, the person is likely to be happier with the results.13

Dose adjustments were made in this study according to gender and severity of glabellar lines, reflecting the true situation for BoNT-A treatment of patients with no specific, standardized dose given. Touch-ups were permitted, which has become the normal practice for many aesthetic treatments with a BoNT-A product. A slightly higher dose was observed for male subjects, consistent with a previous report stating that men have greater muscle mass in the glabellar area than women and therefore require higher doses of BoNT-A.14 As expected, a higher dose was also reported for subjects with severe glabellar lines at baseline.

A high level of subject satisfaction was achieved 3 weeks after the treatment of glabellar lines with BoNT-A (s.U), and was maintained until at least 4 months. Moreover, subjects were highly satisfied with the treatment regardless of their gender or severity of glabellar lines at baseline, whether or not they received a touch-up injection and whether or not they were naive to BoNT-A treatment. Of perhaps the greatest importance, satisfaction with treatment was related to a more positive self-perception. Four months after the injection, only four subjects thought they still looked older than their age whilst the majority (88.6%) felt better about themselves since the injection. Also, while more than one-third of subjects thought the injection brought them more 'youth', in fact 'harmony' and 'self-esteem/confidence' were the two top choices and 'beauty' came only in fourth place. This self-analysis of results from a BoNT-A treatment, expressed in such a way, is a unique finding of the current study.

In this study, more subjects who had previously received injection of another BoNT-A product in their glabellar complex now preferred BoNT-A (s.U) in the current treatment, related both to the aesthetic outcome and duration of effect. This result differed from the findings by de Boule15 which suggested that more subjects preferred their original BoNT-A product to BoNT-A(s.U). Neither of the studies (the present study and that by de Boule15) was randomized and there was no double-blind, head-to-head comparison of the two BoNT-A formulations in terms of patient satisfaction. However, the apparent significant differences in the results obtained could be explained by a number of equally marked differences in the study designs.

Firstly, the scale of the current study was considerably larger, over ten times the de Boule study (533 subjects at 66 centres in 4 European countries). In the present study, the two specific questions comparing BoNT-A products were answered by 244 and 171 subjects, respectively, compared to 40 subjects previously recruited at the single-centre study in Belgium. Also, the current study was designed to mimic the real world situation, in which the patients were the drivers for treatments and determined when they would like to be treated; the investigators just confirmed their eligibility according to the product labelling. Conversely, in the Belgium study, subjects received their injection of BoNT-A (s.U) on average 20 weeks after their previous product injection when the improvement 'started to diminish in the opinion of the investigator'. This would indicate a lack of motivation of the subjects to receive the second treatment session, since that decision was based on the opinion of the investigator and not on the willingness of the subjects. The severity before the injection of BoNT-A (s.U) was not provided in de Boule’s publication. Therefore, it is likely that the glabellar lines before injection were insufficiently severe for the patients to observe a dramatic and satisfying improvement. Finally, the subjects in the present study paid for their own treatments and were not compensated for their participation in the study. All eligible subjects were consecutively proposed for enrolment into the study.
study and the auto-questionnaires were completed by the subjects at home and mailed back directly with the results remaining confidential to the investigators. These procedures, as defined in the study protocol, in our opinion have helped to minimize the bias of subjects and the conscious or unconscious influence of the investigator on the satisfaction and preference of the subjects about the treatments.

In summary, we have demonstrated that, through this large-scale observational study, treatment of the glabellar lines with BoNT-A (s.U) resulted in a high level of satisfaction and corresponded to a more positive self-perception 4 months after injection.

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