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Clinical Research Paper

# A cross-sectional structured survey of patients receiving botulinum toxin type A treatment for blepharospasm☆

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ABSTRACT

To characterize satisfaction with current standard-of-care botulinum neurotoxin type A (BoNT/A) treatment for blepharospasm, we performed a cross-sectional, structured survey in subjects with blepharospasm who had received ≥2 BoNT/A cycles. Subjects were interviewed immediately before re-injection to evaluate treatment satisfaction, time course of treatment effects, preferred injection intervals, Jankovic Rating Scale (JRS), and Blepharospasm Disability Index (BSDI).

Subjects' ($n = 114$) last treatment was onabotulinumtoxinA ($n = 78$), incobotulinumtoxinA ($n = 35$), or abobotulinumtoxinA ($n = 1$). The most frequent injection interval was 12 weeks (46.5% subjects); 30.7% had an interval >12 weeks. The main rationale for interval choice was "to maintain treatment efficacy" (44.7%). However, 36.6% reported that treatment effects usually declined within 8 weeks; 69.6% within 10 weeks. JRS and BSDI scores indicated re-emergence of symptoms before re-injection, with 70.2% and 73.7% of subjects reporting difficulties to drive and read, respectively. Overall, treatment satisfaction was high, but declined at the end of the cycle. Many subjects (52.3%) would prefer an injection interval of <12 weeks; 30.6% of <10 weeks.

In conclusion, the survey results indicate that blepharospasm symptoms, such as difficulties to drive and read, re-emerge at the end of a BoNT treatment cycle and that flexible, individualized treatment intervals may improve treatment satisfaction and outcomes.



## 1. Introduction

Blepharospasm is a focal dystonia characterized by excessive involuntary closure of the eyelids caused by contraction of the *orbicularis oculi* and other facial muscles [1]. Blepharospasm is a chronic, disabling condition that affects patients' quality of life, social interactions, employment status, and may lead to depression [2–5]. With prevalence estimates ranging from 16 per million (in Japan) to 133 per million (in Southern Italy), primary blepharospasm is one of the most common forms of adult-onset dystonia [6]. It predominantly occurs in patients in their fifties and sixties, and affects women more than men [6,7]. It is estimated that at least 50,000 individuals in the USA are affected by blepharospasm, corresponding to a prevalence of approximately 50 per million, with a female preponderance of 1.8:1 [8].

The recommended treatment option for blepharospasm, based on US and European treatment guidelines as well as expert consensus, is repeated intramuscular injections of botulinum neurotoxin (BoNT) [9–11]. In the USA and Europe, three BoNT type A (BoNT/A) formulations (abobotulinumtoxinA, Dysport®, Ipsen Biopharm Ltd., UK; incobotulinumtoxinA, Xeomin®, Merz Pharmaceuticals GmbH, Germany; onabotulinumtoxinA, Botox®, Allergan, Inc., USA) are currently available commercially. At present, all three formulations are licensed for the treatment of blepharospasm in Europe [12–14], while only incobotulinumtoxinA and onabotulinumtoxinA are licensed for the treatment of blepharospasm in the USA [15,16]. These formulations are derived from the Hall strain of *Clostridium botulinum*; in

*Abbreviations:* BoNT, botulinum neurotoxin; BoNT/A, botulinum neurotoxin type A; BSDI, Blepharospasm Disability Index; CD, cervical dystonia; JRS, Self-administered Jankovic Rating Scale; SD, standard deviation.

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incobotulinumtoxinA, the active neurotoxin has been purified from neurotoxin-associated complexing proteins [17].

The efficacy and safety of BoNT/A formulations for the treatment of blepharospasm have been demonstrated in a number of controlled clinical trials [18–24]. However, treatment effects are temporary and patients require repeat injections. Current US and European prescribing information for approved BoNT/A formulations recommend minimum injection intervals of 12 weeks for the treatment of blepharospasm, mainly due to concerns that shorter intervals might promote the development of neutralizing antibodies and adverse events, with eyelid ptosis and dry eyes being described as the most common adverse effects of BoNT/A treatment for blepharospasm [13–16,25]. To date, only one prospective clinical trial has been conducted in blepharospasm allowing BoNT treatment intervals shorter than 12 weeks [19,26]. This study included a randomized, placebo-controlled main period with one incobotulinumtoxinA treatment followed by an open-label extension period with up to five incobotulinumtoxinA treatments at flexible intervals ≥6 weeks, with a total treatment duration of up to 68 weeks. In this study, injection intervals <12 weeks were not associated with a higher incidence of adverse events than intervals ≥12 weeks [27] and no patients developed neutralizing antibodies based on the sensitive mouse hemidiaphragm assay [26]. Importantly, the study also revealed that treatment intervals <12 weeks were clinically indicated in a considerable proportion of patients with blepharospasm, based on the clinical need for re-injection as established by the investigator and confirmed by a Jankovic Rating Scale (JRS) severity subscore ≥2 [26]. Hence, many patients with blepharospasm experienced recurrence of symptoms before the end of the current standard-of-care 12-week interval, which may reduce quality of life.

We conducted a cross-sectional, structured survey in the USA in subjects who received BoNT/A injections for blepharospasm. We assessed BoNT/A treatment history, treatment intervals, physicians' rationale for intervals, time course of patient-reported therapeutic effects, treatment satisfaction, patient-preferred treatment intervals, Blepharospasm Disability Index (BSDI), and self-administered JRS scores.

## 2. Material and methods

### 2.1. Ethics and regulatory requirements

The study protocol, informed consent, and other appropriate study-related documents were reviewed and approved by an independent ethics committee/institutional review board. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and are consistent with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice guidelines and applicable regulatory requirements. Written informed consent was obtained from each subject prior to enrollment (i.e. prior to completing the survey). The trial was registered with ClinicalTrials.gov. (NCT01686061).

### 2.2. Subjects

Subjects who were eligible for participation included 18- to 80-year-old men and women with blepharospasm who had completed ≥2 treatment cycles with abobotulinumtoxinA, incobotulinumtoxinA, or onabotulinumtoxinA. The survey focused on BoNT/A treatment only and subjects were excluded if they had received rimabotulinumtoxinB during any of the previous two treatment cycles.

Subjects were recruited at five clinical sites in the USA. All subjects attending study sites to receive BoNT/A treatment for blepharospasm were invited to enroll. Interviews took place immediately prior to subjects' next scheduled treatment, i.e. just before a re-injection. However, the survey was a non-interventional study and no treatments were administered as part of the study. Survey data were collected via interviews conducted by study staff other than treating physicians; the same member of staff conducted all interviews at each site, whenever possible.

### 2.3. Patient survey

Demographics, baseline disease characteristics, medical history, previous BoNT/A treatment history and reasons for the chosen treatment interval were retrieved from subjects' medical records. The reasons for the chosen treatment interval could be selected from a pre-defined list in the case report form (included as supplementary material), but study staff had the option to specify other reasons if applicable. The study then collected the following information about subjects' perspectives of BoNT/A treatment.

#### 2.3.1. Botulinum toxin treatment – historical and current cycle

Subjects were asked to recall their BoNT/A treatment history (usual treatment interval, reasons for the interval, and usual time to onset, peak, and decline in effect) and experiences over the current injection cycle (time to onset, peak, and decline in effect). Subjects were asked when they would have preferred to have their next injection, if given the choice.

#### 2.3.2. Treatment satisfaction

Subjects rated their current satisfaction with BoNT/A treatment using a numerical rating scale ranging from 1 to 10, where 1 was defined as *not at all satisfied* and 10 as *very satisfied*. Subjects were also asked to recall their satisfaction at the peak effect of BoNT/A treatment during their current cycle. Subjects with a rating of 1–3 were classified as *not at all satisfied*, those with a rating of 4–7 as *somewhat satisfied*, and those with a rating of 8–10 as *very satisfied*.

#### 2.3.3. Blepharospasm disability index

Subjects completed the BSDI, a validated scale assessing functional impairment in activities of daily living [21,28]. Items were rated on a 5-point scale from 0 (no impairment) to 4 (no longer possible due to blepharospasm), or rated as non-applicable. Subjects were also asked to recall their level of impairment at the peak of BoNT/A treatment effect.

#### 2.3.4. Jankovic rating scale

The JRS is a validated physician rating scale that includes a severity item and a frequency item that are both scored from 0 (best) to 4 (worst) [18,28]. In this survey, we have used the JRS as a self-administered instrument that was completed by subjects under the guidance of clinic staff to rate blepharospasm symptoms (current and at the peak of BoNT/A treatment effect).

### 2.4. Statistical methodology

Descriptive statistics were used to summarize all data. Continuous variables were summarized by number, mean and standard deviation (SD), and median value and range. Categorical variables were summarized as counts and percentages. Percentages were based on non-missing values. Statistical analysis was performed using the SAS® software package (SAS Institute Inc., Cary, NC).

## 3. Results

The survey took place between September 2012 and April 2013. Overall, 124 subjects participated in the survey and 91.9% (114/124) were included in the final analysis. The other 8.1% of subjects (10/124) were excluded as they had not met the inclusion criterion for age.

**Table 1**
Demographics, baseline disease characteristics, and treatment history.

| Characteristic | Subjects $N = 114$ |
|---|---|
| Female gender, n (%) | 80 (70.2) |
| Mean (SD) age, years | 66.1 (8.8) |
| Median (range) duration of blepharospasm, months | 120 (12–900) |
| Type of blepharospasm,[a] n (%) | |
| Mixed (clonic/tonic) | 68 (59.7) |
| Primarily tonic | 22 (19.3) |
| Primarily clonic | 24 (21.1) |
| Comorbid chronic diseases requiring medical management,[b] n (%) | |
| Any condition | $N = 95$ (83.3) |
| Hypertension | 47 (49.5)[c] |
| High cholesterol | 41 (43.2)[c] |
| Thyroid problem | 28 (29.5)[c] |
| Diabetes | 21 (22.1)[c] |
| Depression/suicide | 15 (15.8)[c] |
| Cancer (malignancy) | 7 (7.4)[c] |
| Asthma | 6 (6.3)[c] |
| Congenital heart disease | 6 (6.3)[c] |
| Median (range) duration of BoNT/A treatment, months | 96 (6–312)[d] |
| Last BoNT/A formulation given, n (%); mean (SD) dose | |
| OnabotulinumtoxinA | 78 (68.4); 71.8 (30.1) units |
| IncobotulinumtoxinA | 35 (30.7); 76.4 (26.4) units |
| AbobotulinumtoxinA | 1 (0.9); 100.0 (−) units |

BoNT/A = botulinum neurotoxin type A; SD = standard deviation.
[a] Clonic blepharospasm is characterized by alternating contraction and relaxation of the *orbicularis oculi* while tonic blepharospasm is characterized by sustained contraction.
[b] Subjects may have had more than one condition. Conditions occurring in >5% of subjects are listed.
[c] Percentages are based on the number of subjects with comorbid conditions ($n = 95$).
[d] Data available for 113 subjects.

### 3.1. Baseline characteristics and BoNT/A treatment history

Subjects were aged 28–80 years (mean 66.1 [SD 8.8] years) with a median duration of blepharospasm of 120 months. Most subjects (70.2%, 80/114) were female. The majority of subjects (83.3%, 95/114) had other chronic diseases requiring medical management (Table 1).

Subjects had received BoNT/A injections for blepharospasm for a median of 96 months. Table 1 also summarizes the BoNT/A formulations and doses that subjects had received as their last treatment.

### 3.2. Time to onset, peak, and waning of BoNT/A treatment effect

Ninety-three percent of subjects (106/114) recalled usually experiencing onset of treatment effect within 1 week of an injection for their previous treatments, with the remainder experiencing onset within 2 weeks; 90.2% (101/112) recalled reaching the maximum or peak effect in the first 4 weeks after an injection. Although the majority of subjects (69.6%, 78/112) reported that treatment effects declined within 10 weeks of an injection and 36.6% (41/112) usually felt effects declining within 8 weeks, waning of effect could also be reported as late as 20 weeks post-injection (Fig. 1).

A very similar pattern was seen when subjects were asked about their current treatment cycle specifically. In summary, 92.9% of subjects (105/113) felt the onset of effect within 2 weeks of treatment and 81.4% (92/113) reported experiencing the peak effect within 4 weeks. Treatment effects began to wear off within 10 weeks of the injection for 69.6% of subjects (78/112) and within 8 weeks for 35.7% (40/112). One subject reported that no treatment effect had been present during the current cycle.

### 3.3. Current BoNT/A treatment intervals

Information from subjects' medical records showed injections were most frequently received at 12-week intervals (46.5%, 53/114). Nearly one-third of subjects (30.7%, 35/114) had repeat injections at intervals >12 weeks, including 3 subjects with intervals of 24 weeks. For the remaining 22.8% of subjects (26/114), the treatment interval was <12 weeks (Fig. 2). Overall, the mean (SD) treatment interval based on the patient survey was 12.5 (3.3) weeks (median 12 weeks; range 3–24 weeks,).

From the subjects' medical records, the reasons physicians had chosen a subject's treatment interval were "maintain efficacy" (44.7%, 51/114), "standard procedure" (37.7%, 43/114), "insurance approval guidelines" (15.8%, 18/114), "scheduling" (0.9%, 1/114), and "subject does not need injection sooner" (0.9%, 1/114). These data were in good agreement with the reason subjects recalled having been told by their physicians: "maintain efficacy" (59.6%, 62/104), "standard procedure" (20.2%, 21/104), "insurance approval guidelines" (17.3%, 18/104), "scheduling" (1.0%, 1/104), "when the patient needs it" (1.0%, 1/104), and "frequent eye closure and spasms" (1.0%, 1/104). Ten subjects stated they had not been given a reason for their treatment interval. Only one reason was recorded for each subject.

### 3.4. Treatment satisfaction

At the time of the interview, 56.1% of subjects (64/114) were at least *somewhat satisfied* with BoNT/A treatment for blepharospasm, while

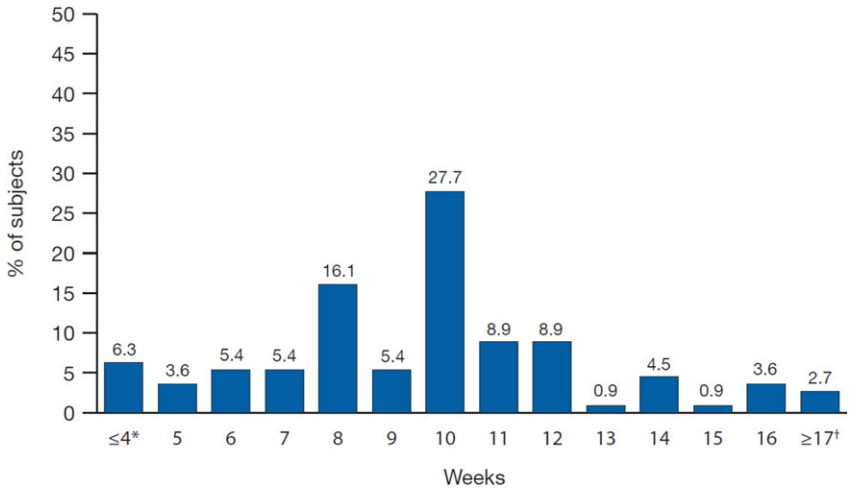


**Fig. 1.** Time to subject-reported decline in botulinum neurotoxin type A treatment effect ($n = 112$). Subjects were asked: "Over the course of all of your botulinum toxin treatments, in general, when do you usually feel a considerable decline in the effect of the botulinum toxin?". *1 subject reported effects usually decline within 1 week, 2 subjects within 2 weeks, and 4 subjects within 4 weeks. †2 subjects reported effects usually decline 18 weeks after treatment and 1 subject reported a decline 20 weeks after treatment.

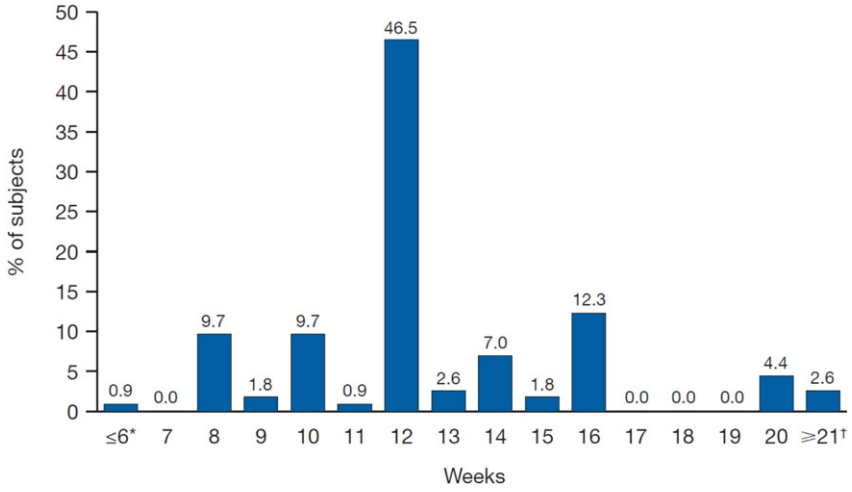


**Fig. 2.** Botulinum neurotoxin type A treatment intervals (from medical records) ($n = 114$). Intervals with which the subject normally receives botulinum toxin injections, based on medical records. *1 subject received intervals of 3 weeks. †3 subjects received intervals of 24 weeks.

97.3% of subjects (110/113) recalled being at least *somewhat satisfied* at the peak of BoNT/A treatment effects (Table 2).

### 3.5. Preferred injection intervals

When asked how often they would prefer to receive BoNT/A treatment, the most frequent interval was 12 weeks (24.3%, 27/111) (Fig. 3). However, most subjects (52.3%, 58/111) would prefer intervals <12 weeks, including 30.6% of subjects (34/111) who would prefer intervals <10 weeks. Nearly a quarter of subjects (23.4%, 26/111) would prefer intervals >12 weeks.

### 3.6. Blepharospasm disability index

At the time of the interview, 60.5% (69/114) to 73.7% (84/114) of subjects reported impairment when performing activities of daily living, or an inability to perform these activities at all. At the peak of therapy effect of the current cycle, 28.9% (33/114) to 38.6% (44/114) of subjects recalled impairment or inability to perform activities of daily living (Fig. 4).

### 3.7. Jankovic rating scale

Based on self-assessments, the mean (SD) JRS severity and frequency scores at the time of the interview were 3.55 (1.07) and 3.43 (0.99), respectively, indicating severe symptoms. At the time of peak effect of the current cycle, the mean (SD) JRS severity and frequency scores were 2.18 (0.93) and 2.20 (1.03), respectively (Fig. 5).

**Table 2**
**S**atisfaction with botulinum neurotoxin type A treatment.

| | Just prior to re-injection ($n = 114$) | At the peak of treatment effect[a] ($n = 113$) |
|---|---|---|
| Very satisfied (NRS 8–10), n (%) | 30 (26.3) | 100 (88.5) |
| Somewhat satisfied (NRS 4–7), n (%) | 34 (29.8) | 10 (8.8) |
| Not at all satisfied (NRS 1–3), n (%) | 50 (43.9) | 3 (2.7) |
| Mean (SD) satisfaction score | 6.2 (2.9) | 8.8 (1.7) |

Subjects were asked "How satisfied are you at the moment with the current effect of your medication?" and "Compared to your current satisfaction with the effect of your medication, how satisfied were you when you felt the strongest effect of the medication?".
NRS = numerical rating scale; SD = standard deviation.
[a] Based on subject recollection at the time of the interview, i.e. just prior to re-injection.

## 4. Discussion

Blepharospasm is often a disabling condition that significantly reduces patients' quality of life [2–5]. Treatment with BoNT/A injections temporarily reduces the symptoms of blepharospasm, is well tolerated, and may improve quality of life [18–24]. This structured survey was carried out to assess real-world treatment history, treatment intervals, patient satisfaction with treatment, time course of BoNT/A treatment effects, preferred injection intervals, disability, and disease severity of subjects who had received ≥2 complete cycles of BoNT/A treatment for blepharospasm. The final analysis included 114 subjects who, on average, had had a diagnosis of blepharospasm for more than 10 years and had been treated with BoNT/A for most of that time. Most subjects were women, reflecting the higher prevalence of blepharospasm in females. The subjects included had a mean age of 66.1 years and, as expected in a population of that age, the majority (83.3%) had other chronic diseases requiring medical treatment.

Approximately two-thirds of the subjects received onabotulinumtoxinA injections, and one-third received incobotulinumtoxinA. The mean doses of onabotulinumtoxinA (71.8 U) and incobotulinumtoxinA (76.4 U) administered at the last treatment were similar for both formulations and in accordance with the products' labeling information [13–16]. One subject had received abobotulinumtoxinA, a formulation that is not currently licensed for the treatment of blepharospasm in the USA. The most frequent treatment interval was 12 weeks (46.5% of subjects) as recommended by current product labeling, with nearly a third of subjects (30.7%) receiving treatment at intervals >12 weeks. Less than a quarter of subjects (22.8%) received treatment at intervals shorter than recommended by current product labeling.

When asked about the time course of treatment effects, the vast majority of subjects stated that they usually felt the onset of treatment effect in the first week and reached the peak of therapy effect within the first 4 weeks after treatment. However, there was noticeably more variability between subjects in the time to waning of treatment effect. Most subjects felt a considerable decline in BoNT/A treatment effects within 8 to 10 weeks after injection. Given that 77.2% of subjects received treatment at intervals of ≥12 weeks, these data suggest that most subjects usually received re-injections after BoNT/A treatment effects have begun to wane and therefore may have experienced recurrent blepharospasm symptoms toward the end of each injection cycle. This was reflected in the BSDI and JRS assessments, showing that, at the time of the interview, many subjects experienced functional impairment due to recurrence of blepharospasm symptoms compared with the peak of therapy effect. As a result, satisfaction with BoNT/A

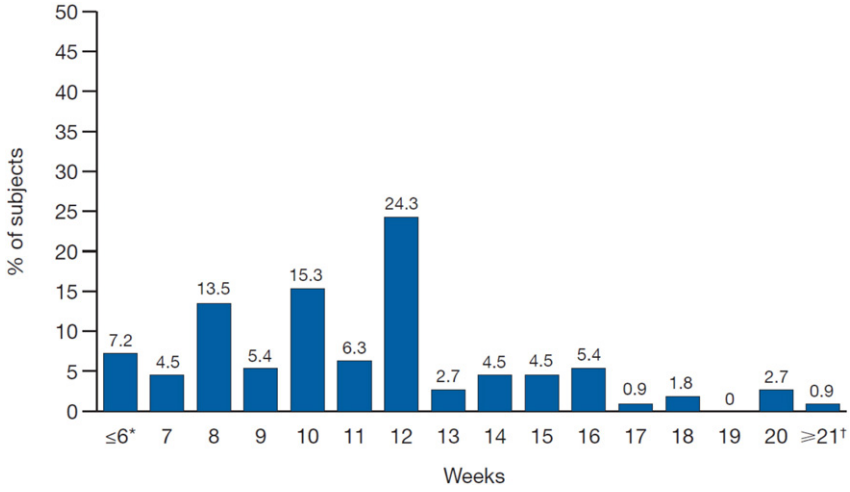


**Fig. 3.** Subject preference for botulinum neurotoxin type A treatment intervals ($n = 111$). Subjects were asked: "If given the choice, when would you have preferred to have your next injection?". *2 subjects preferred intervals of 1 week, 1 subject intervals of 2 weeks, 1 subject intervals of 4 weeks, and 4 subjects intervals of 6 weeks. †1 subject preferred intervals of 24 weeks.

treatment, which was rated as high at the peak of therapy effect, declined at the time of the interviews, which were conducted just before a re-injection. It is important to note that the retrospective BSDI and JRS assessments both indicated that even at the time of peak effect, subjects still considered themselves to have significant symptoms.

Our survey revealed that approximately half of all subjects (52.3%) would prefer to receive BoNT/A treatment at intervals <12 weeks, with nearly a third of all subjects (30.6%) preferring intervals <10 weeks. However, it needs to be borne in mind that almost a quarter of subjects (23.4%) preferred injections at >12-week intervals showing how patient preferences varied over a wide range of treatment intervals. These data are similar to patient preferences found in surveys of patients who received onabotulinumtoxinA or abobotulinumtoxinA treatment for dystonia [29], and of patients who received any of the three BoNT/A preparations for spasticity [30]. Both studies concluded that patient satisfaction with BoNT/A declined toward the end of the injection cycle and that many patients would like to be treated more frequently than the intervals they received.

The 12-week standard-of-care BoNT/A treatment interval for blepharospasm (and other indications) that is recommended in the current product labeling of BoNT/A formulations is partly based on a retrospective study, where shorter injection intervals were associated with secondary non-response to BoNT/A in subjects with cervical dystonia (CD) [31]. However, the study included only eight non-responders and only three of those had serological evidence for neutralizing antibodies against BoNT/A. In addition, the subjects in this study had been treated with the original botulinum toxin formulation (Allergan lot 79–11), which has since been shown to be more immunogenic than later formulations of onabotulinumtoxinA [32]. Hence, the relevance of these early findings for modern BoNT/A formulations is unclear.

More recently, the efficacy and safety of individualized treatment regimens have been evaluated in two prospective clinical trials investigating repeated incobotulinumtoxinA treatments for patients with blepharospasm [19,26] and patients with CD [33,34]. Both studies included a randomized, placebo-controlled main period during which subjects could receive one treatment with incobotulinumtoxinA or placebo, followed by an open-label extension period in the blepharospasm study or a randomized double-blind period in the CD study. Overall, subjects could receive up to six incobotulinumtoxinA injections at

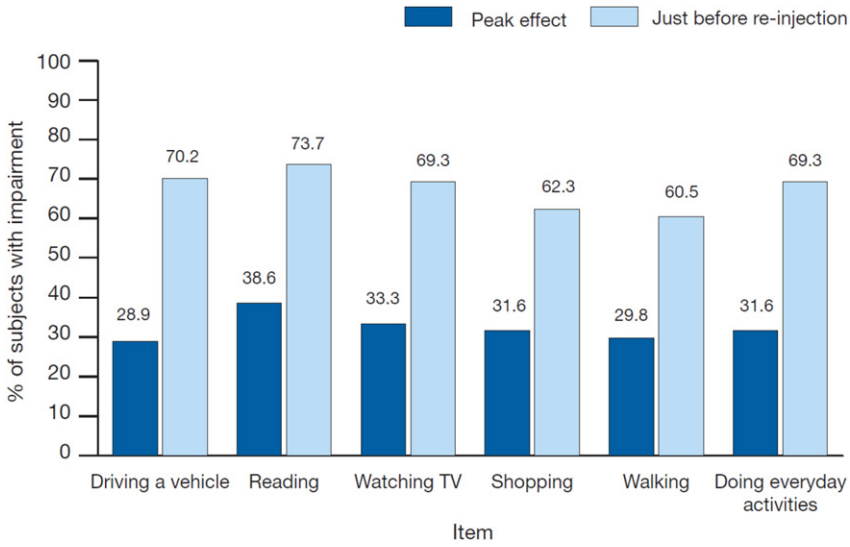


**Fig. 4.** Subject-reported Blepharospasm Disability Index ($n = 114$). Subjects rated items on a 5-point scale from 0 (no impairment) to 4 (no longer possible due to blepharospasm), or rated them as non-applicable. Data shown are the percentage of subjects with a score of ≥1 (slight impairment or worse) for each item.

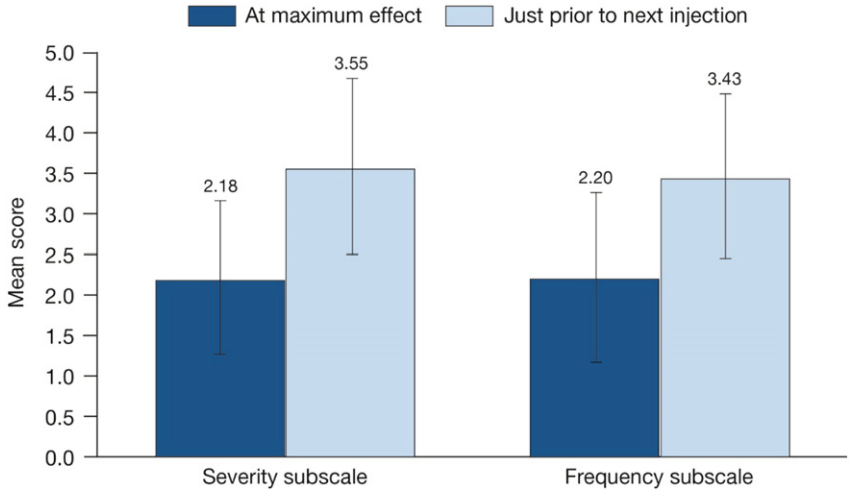


**Fig. 5.** Subject-reported mean JRS severity and frequency scores ($n = 114$). JRS frequency and severity scores range from 0 (best) to 4 (worst). Error bars represent the standard deviation.

intervals of at least 6 weeks if there was a clinical need for re-injection, assessed by a physician using a validated clinical rating scale (JRS or Toronto Western Spasmodic Torticollis Rating Scale). A detailed post-hoc analysis showed that in the blepharospasm study, 44.9% of treatments were administered at injection intervals <12 weeks and 26.5% of injections were administered at intervals <10 weeks, which are very similar to the intervals preferred by subjects in this survey. Importantly, there were no differences in the overall incidence of adverse events or in the incidence of the most frequent adverse events (dry eyes, ptosis, and dry mouth), regardless of the incobotulinumtoxinA treatment interval [27]. Similar results were seen in the CD survey and clinical trial [27,29].

In this survey, the most important reason for the choice of BoNT/A treatment interval was "to maintain treatment efficacy". This was in contrast to the BSDI and JRS assessments, which suggested that efficacy was not optimally maintained toward the end of the treatment cycle for many subjects. The analysis by Evidente et al. confirmed that many patients who receive BoNT/A injections for blepharospasm have a clinical need for re-injection <12 weeks after the previous treatment, based on JRS assessments carried out by trained physicians [27]. It is important to consider that the survey recorded only one reason for the choice of treatment interval for each patient. This is potentially an important limitation of this study since in clinical practice, physicians' decisions are based on a number of factors, including insurance approval guidelines. However, insurance guidelines may not be recorded in medical records as part of the rationale for choosing the treatment interval and may not be communicated to patients. Hence, the survey may underestimate the influence of insurance approval guidelines on the choice of treatment intervals in real-world practice.

Although the patient survey provides useful insight into the real-world use and treatment satisfaction with BoNT/A, there are some methodological limitations that need to be considered to contextualize the findings. Only one reason for the chosen treatment interval was recorded. Subjects' responses were based on recollection of their treatment experiences in general and their last treatment cycle in particular. The JRS assessments were self-administered under the guidance of clinic staff rather than conducted by trained investigators. In addition, the small sample size may limit the generalization of results to all patients with blepharospasm and does not allow examination of potential predictors either of treatment satisfaction or the time course of treatment effects, and potential correlations between these variables. Further studies allowing such analyses may be able to identify subsets of patients with blepharospasm who are most likely to benefit from shorter treatment intervals.

## 5. Conclusions

To our knowledge, this survey is the most comprehensive study investigating patients' preferences and treatment satisfaction with BoNT/A treatment for blepharospasm to date. The survey revealed that, overall, patient satisfaction with BoNT/A treatment regimens for blepharospasm was very high. However, toward the end of the treatment cycle, functional impairments and disability due to blepharospasm, e.g. difficulties with everyday activities such as driving and reading, worsened and patient satisfaction declined. More than half of the patients surveyed expressed a desire to receive injections more frequently than the current standard-of-care 12-week interval, suggesting that more flexible, individualized treatment intervals may improve treatment satisfaction and outcomes for patients with blepharospasm.

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## Declaration of financial/other relationships

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jns.2016.05.033.

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