Long-Term Safety Review of Subjects Treated With Botulinum Toxin Type A for Cosmetic Use

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ABSTRACT

The use of botulinum toxin type A for treating hyperfunctional facial lines has expanded the treatment options for facial aesthetic procedures. This study assessed the long-term safety associated with botulinum toxin type A treatment of facial rhytids. Fifty subjects were enrolled in this retrospective chart review. Key enrollment criteria were: 18 years of age or older at first treatment, first treatment prior to January 1, 1999, complete dose information in charts, a history of at least 10 treatments with the same investigator, and exclusive use of the same brand of botulinum toxin type A. Demographic data, relevant medical history, details of botulinum toxin type A treatment, discontinuations, and all adverse events (AEs) were compiled from charts of eligible subjects. The mean age of the 50 subjects was 42.8 years; 92% were women; and medical histories were unremarkable. The main reasons for botulinum toxin type A treatment were glabellar rhytids (n=49), crow's feet (n=35), and forehead rhytids (n=32). Most subjects received treatment in multiple areas: 82% received treatment in 2 areas or more, and 68% received treatment in 3 areas or more. The median number of treatment sessions was 19 (range, 10 to 30), the median cumulative dosage was 690 U (range, 244 to 1603), the median dose per treatment session was 40 U, and the median duration of time between the first and last treatment was 5.95 years (range 2.82 to 8.99). The majority of subjects (n=42, 84%) did not report any AEs. Eight subjects reported a total of 10 AEs. Five of the AEs (2 bilateral eyebrow ptosis, 1 right eyebrow ptosis, 1 right eyelid ptosis, 1 dysphagia) were considered to be definitely related to botulinum toxin type A treatment. None of the 10 AEs was severe and all were transient. Of the 8 subjects reporting AEs, most (6) had 1 event. Of the 853 treatment sessions, 99% were not associated with AEs. The risk of AEs did not appear to increase with the number of treatments or be related to the interval between treatments. This retrospective analysis demonstrates that botulinum toxin type A treatment for facial aesthetic procedures has proven safety and is well-tolerated in the long term when used in multiple treatment sessions over periods extending up to 9 years.

INTRODUCTION

- Botulinum toxin type A injection is the most common nonsurgical cosmetic procedure in the United States[1]
- More than 2.2 million botulinum toxin type A procedures were undertaken in 2003, the latest year for which data are available[1]
- Botulinum toxin type A injections can be performed in the office setting with a high degree of safety and minimal discomfort to the subject
- Due to its mechanisms of action, effects of botulinum toxin type A last for approximately 3 to 4 months and then retreatment is necessary
- Therefore, it was deemed important to evaluate the safety of botulinum toxin type A over the long term in subjects who had undergone multiple treatments

OBJECTIVE

- To assess the long-term safety of botulinum toxin type A in subjects with facial rhytids

METHODS

Study Design

- This was a single center, retrospective chart review study (N=50)

Subject Selection Criteria *(Table 1)*

Table 1. Subject Selection Criteria

- Male or female subjects who had been treated for facial rhytids exclusively with the same brand of botulinum toxin type A
- At least 18 years of age at first botulinum toxin type A treatment
- Received first botulinum toxin type A treatment before January 1, 1999
- Received at least 10 injections of botulinum toxin type A for cosmetic use
- Had complete dosing information available for each treatment
- Received all injections from the current investigator
- Able to provide informed consent

Study Protocol

- The investigator compiled a list of all subjects who had received their first injection of botulinum toxin type A for cosmetic use before January 1999
- After screening according to the selection criteria, potential subjects were contacted. The study objective was described and written informed consent was obtained from those who wished to participate
- Data collected from each subject's chart included:
  - Demographics
  - Relevant medical history
  - Indication for botulinum toxin type A treatment
  - Date and dose of each botulinum toxin type A treatment
  - Reason for discontinuation (if it occurred)
  - All adverse events (AEs) occurring during treatment period: event description, severity, relation to botulinum toxin type A treatment, onset date, end date, outcome, and use of concomitant medications

Statistical Analyses

- Descriptive statistics were used to characterize the populations and the data
- Wilcoxon Rank-Sum Test was used to compare characteristics of sessions with and without AEs

RESULTS

Subject Demographics and Medical History

- Fifty subjects met inclusion criteria. Their demographics are found in Table 2

Table 2. Demographics of Subjects at First Botulinum Toxin Type A Treatment (N=50)

Age (years)		Sex, number (%)		Race, number (%)	
Mean	42.8 ± 8.9	Women	46 (92)	White	46 (92)
Median	42	Men	4 (8)	Asian	1 (2)
Range	27–69			Not specified	3 (6)

The medical history of subjects was unremarkable. The most common conditions reported were dermatologic (66% of subjects), relevant allergies (36%), and head, eye, ear, nose, and throat (16%).

Characteristics of Treatment With Botulinum Toxin Type A

- The total number of treatment sessions for all 50 subjects was 853
- The median number of sessions per subject was 19, and the range was 10 to 30
- The median cumulative dose was 690 U (range, 244 to 1603)

Treatment Data

- The majority of subjects received treatment for the upper face: 49 (98%) for glabellar rhytids, 35 (70%) for crow's feet, and 32 (64%) for forehead rhytids
- Correspondingly, the large majority of the 853 treatment sessions were for glabellar rhytids (85.5%). Crow's feet were treated in 46% of sessions, and forehead rhytids in 35% of sessions
- Of the 50 subjects, 9 (18%) received treatment for 5 or more reasons, 11 (22%) received treatment for 4 reasons, 14 (28%) for 3 reasons, 7 (14%) for 2 reasons, and 9 (18%) for 1 reason
- Of the 853 treatment sessions, 41.5% were undertaken for 1 reason and 53% for 2 and 3 reasons

Treatment-Session Intervals

- The median interval between the first and last botulinum toxin type A treatment was 5.95 years. The range was 2.82 to 8.99 years. Data on the intervals between ongoing treatments are shown in Table 3

Table 3. Intervals (in Weeks) Between Treatment Sessions

Sessions	N	Mean ± SD	Median	Range	*P*
All	800	19.3 ± 13.3	17.1	0.43 – 155.3	
With AEs	9	15.6 ± 3.7	15.4	10.4 – 21.3	NS*
Without AEs	791	19.3 ± 13.4	17.1	0.43 – 155.3	NS*

*Wilcoxon Rank-Sum Test.

- The median interval between sessions was 17 weeks and 99% of these treatment sessions occurred without AEs
- Average length of treatment intervals did not differ between treatment sessions in which AEs occurred and those in which they did not

Dosage of Botulinum Toxin Type A

- The median dose of botulinum toxin type A per session was 40 U
- 99% of dosages were not accompanied by AEs, and the range of dosages was substantial for all sessions (2 U to 110 U)

Long-Term Safety

Botulinum toxin type A injections were associated with an excellent safety record in the long term:

- AEs occurred in 9 of 853 sessions (1.1%)
- AEs probably or definitely related to botulinum toxin type A occurred in only 5 (0.6%) sessions

In all, 8 subjects reported a total of 10 AEs:

- 6 subjects reported 1 AE each; 2 subjects reported 2 AEs each
- 5 of the AEs in 4 of the subjects were considered to be probably or definitely drug related. The safety profile of botulinum toxin type A is summarized in Table 4
- None of the 10 AEs was considered serious. AEs that were considered botulinum toxin type A-related did not differ in severity from those that were not drug related. All AEs were mild (80%) to moderate (20%) in severity
- All AEs were transient and there were no sequelae

Table 4. Adverse Events Reported by 8 of 50 Subjects in 853 Treatment Sessions: Relationship to Botulinum Toxin Type A Treatment

Relationship of AE to Treatment (Number of Events)	Description	Severity	Mean Dose of Botulinum Toxin Type A at Session in Which AEs Occurred
Probably or definitely related (n=5)	Bilateral eyebrow ptosis (n=2) Right brow ptosis (n=1) Right eyelid ptosis (n=1) Dysphagia (n=1)	Mild (n=4) Moderate (n=1)	66.2 U
Unrelated (n=5)	Injection pain/discomfort (n=3) Bruising (n=2)	Mild (n=4) Moderate (n=1)	67.8 U

CONCLUSIONS

In this retrospective chart review of botulinum toxin type A treatment for aesthetic reasons, data from 50 subjects were reviewed. The records encompassed 853 treatment sessions over a period ranging from approximately 3 years to 9 years. The results of this analysis confirm the excellent safety profile and tolerability of botulinum toxin type A when it is used in multiple treatment sessions over the long term.

REFERENCE

1. American Society for Aesthetic Plastic Surgery. Quick Facts: Highlights of the ASAPS 2003 Statistics on Cosmetic Surgery. Available at: http://www.surgery.org/download/2003-stats.pdf. Accessed June 15, 2003.

It should be noted that the results reported in this study refer to the Allergan, Inc., formulation of botulinum toxin type A and cannot be generalized to other formulations or serotypes of botulinum toxin. Botulinum toxin type A is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients ≤65 years of age. All other uses are considered off-label. The full prescribing information should be viewed prior to using any products discussed here.

Authors are consultants for Allergan, Inc.

Authors received research grant support from Allergan, Inc., for this study and support for development of this poster.

Presented at the American Academy of Dermatology meeting, Academy '04, July 28-August 1, 2004, New York, NY.