# Effectivity of Dysport® in Patients with Blepharospasm and Hemifacial Spasm who Experienced Failure with Botox®

Samih Badarny MD[1,2], Zvi Susel MD[1] and Silvia Honigman MD[1,2]

[1]Movement Disorders Clinic, Neurology Department, Lady Davis Carmel Medical Center, and [2]Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

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## Abstract

**Background:** Long-term therapy with botulinum toxin is sometimes associated with therapy failure following repeated injections of the neurotoxin, presumably due to specific antibody production. Primary therapy failure with botulinum toxin is less common and poorly understood.

**Objectives:** To examine the effectiveness of the botulinum neurotoxin Dysport® in patients with blepharospasm and hemifacial spasm after primary or secondary failure with Botox® treatments.

**Methods:** In this case series study, eight patients with blepharospasm and hemifacial spasm who experienced primary or secondary therapy failure with Botox were treated with Dysport. In order to render an equivalent Dysport dose, a conversion ratio of 1:3 to 1:4 Botox /Dysport was used.

**Results:** Two patients, one with blepharospasm and the other with hemifacial spasm, who showed primary therapeutic failure with Botox showed good response to Dysport treatments. One patient with tardive blepharospasm did not respond to either drug. Two patients with blepharospasm and three patients with hemifacial spasm who experienced Botox secondary therapy failure responded well to Dysport treatments.

**Conclusions:** Botox and Dysport are both serotype A botulinum toxins but carry different characteristics of biological activity. These differences possibly account for the favorable therapeutic response to Dysport in patients with hemifacial spasm or blepharospasm following failure with Botox treatments.

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The serotype A botulinum toxin Botox® (Allergan, USA) has been widely used for the treatment of blepharospasm and hemifacial spasm. Although the efficacy of Botox is generally good, various responses to repeated treatments over time are common among patients with focal dystonia or hemifacial spasm. Long-term treatment with botulinum toxin results in antibody production against the neurotoxin in 5% of patients with cervical dystonia [1]. This antibody reaction correlates with high doses and high frequency of botulinum toxin treatments and partially explains the secondary therapy failure with botulinum toxin [2,3]. Primary therapy failure with Botox in patients with focal dystonia is less common and often caused by technical inaccuracies [4].

Dysport® (Medison, UK) is another serotype A botulinum toxin. Head-to-head randomized trials comparing Botox with Dysport showed that these two drugs are not bioequivalent, with a Botox/Dysport conversion ratio of between 1:3 and 1:5 commonly used in clinical practice [5]. This study aimed to assess the efficacy of Dysport in patients with blepharospasm and hemifacial spasm who had shown primary or secondary therapy failure with Botox.

## Patients and Methods

Four patients with idiopathic blepharospasm and four patients with hemifacial spasm, aged 61–78, four of them males and four females, were treated and followed in the Movement Disorder Clinic of Carmel Medical Center in Haifa. All patients were injected with Botox or Dysport at 3 month intervals by the same physician (S.B.). Patients who experienced primary (n=3) or secondary (n=5) treatment failure with Botox were treated with repeated Dysport injections using 1:3 and 1:4 Botox/Dysport conversion ratio [7,8], referred to as the last Botox dose before failure. Dysport was initiated at least 3 months after the last Botox injection. Assessment was performed 3 weeks and 3 months after injections. Primary treatment failure was defined as lack of response to three consecutive injections in increment and maximal dose. Secondary failure was defined as gradual decline in response to Botox despite dosage increase after repetitive treatments at 3 month intervals.

Efficacy of treatments was assessed using a 0 to 4 modified Jankovic rating scale [6] for severity and frequency of blepharospasm and hemifacial spasm, with 0 indicating no signs and 4 maximal severity [Table 1], and a 0 to 3 scale for subjective improvement in symptoms, with 0 indicating no improvement and 3 maximal improvement [Table 2].

## Results

Doses of Botox treatments ranged from 15 to 100 U, and treatment duration ranged from 6 months to 8 years with 3–20 repeated treatments [Tables 1 and 2].

Two patients with idiopathic blepharospasm (patients 1 and 3) and one patient with hemifacial spasm (patient 2) had primary failure with Botox. Patient 3 failed to respond to Dysport as well. Patients 1 and 2 exhibited good response to Dysport in severity and symptom frequency (reduction down to 0–1 in the Jankovic rating scale) and gained 2 to 3 points in the subjective improvement scale.

Two patients with idiopathic blepharospasm (patients 4 and 5) and three patients with hemifacial spasm (patients 6, 7 and 8) had secondary failure with Botox. These patients showed a moderate to good response to Dysport in severity and good

**Table 1.** Comparison of blepharospasm and hemifacial spasm response to Botox and Dysport: modified Jankovic rating scale

| Patient #, gender, age (yrs) | Disorder, disease duration | | Before Botox* | After Botox* | After Dysport* | Botox dose, duration & no. of treatments | Dysport dose & no. of subsequent treatments*** |
|---|---|---|---|---|---|---|---|
| 1, | Blepharospasm, | Severity | 3 | 3 | 0 | 40–80 U** 6 months | 240 U |
| male, 61 | 6 yrs | Frequency | 3 | 3 | 1 | 3 treatments | 5 treatments |
| 2, | Hemifacial spasm, | Severity | 4 | 4 | 1 | 15–35 U** 6 months | 100 U |
| female, 78 | 4 yrs | Frequency | 3 | 3 | 1 | 3 treatments | 2 treatments |
| 3, | Blepharospasm, | Severity | 4 | 4 | 4 | 50–100 U** 1 year | 300–500 U** |
| male, 65 | 15 yrs | Frequency | 4 | 4 | 4 | 5 treatments | 3 treatments |
| 4, | Blepharospasm, | Severity | 3 | 0–3 | 2 | 50–85 U** 8 years | 250 U |
| female, 73 | 12 yrs | Frequency | 3 | 1–2 | 1 | 20 treatments | 4 treatments |
| 5, | Blepharospasm, | Severity | 3 | 0–3 | 0 | 50–85 U** 3 years | 250 U |
| female, 63 | 7 yrs | Frequency | 2 | 0–2 | 0 | 6 treatments | 5 treatments |
| 6, | Hemifacial spasm, | Severity | 3 | 1–3 | 1 | 20–35 U** 5 years | 100 U |
| female, 72 | 8 yrs | Frequency | 3 | 1–3 | 1 | 10 treatments | 5 treatments |
| 7, | Hemifacial spasm, | Severity | 3 | 1–3 | 1 | 40 U 6 years | 120 U |
| male, 62 | 9 yrs | Frequency | 3 | 1–3 | 1 | 10 treatments | 6 treatments |
| 8, | Hemifacial spasm, | Severity | 4 | 1–4 | 1 | 25–30 U** 4 years | 100 U |
| male, 75 | 7 yrs | Frequency | 3 | 1–3 | 2 | 7 treatments | 3 treatments |

* Severity and frequency score: 0 = no sign, 4 = highest

** Dose per treatment from first to last injection

*** Number of treatments until end of the study.

**Table 2.** Comparison of blepharospasm and hemifacial spasm patients' response to Botox and Dysport – a subjective scale of symptomatic improvement

| Patient # | Disorder | After Botox | After Dysport |
|---|---|---|---|
| 1 | Blepharospasm | 0 | 3 |
| 2 | Hemifacial spasm | 0 | 2 |
| 3 | Blepharospasm. | 0 | 0 |
| 4 | Blepharospasm. | 2–0** | 2 |
| 5 | Blepharospasm. | 3–1** | 3 |
| 6 | Hemifacial spasm | 2–0** | 2 |
| 7 | Hemifacial spasm | 2–1** | 2 |
| 8 | Hemifacial spasm | 2–0** | 2 |

* 0 = no improvement, 3 = highest improvement

** From first to last injection.

response in symptom frequency (reduction down to 0–2 and 0–1, respectively in the Jankovic rating scale) and gained 2 to 3 points in the subjective improvement scale.

The response to Dysport was determined after the first injection, and subsequent treatments were required every 3 months to maintain effective results (except for patient 3 who did not respond to repeated Dysport injections).

## Discussion

Both Botox and Dysport are serotype A botulinum toxins but differ in their characteristics. Most studies show similar efficacy of the two products in hemifacial spasm and blepharospam when a 1:3 to 1:5 conversion ratio is used, though with a large variability in various parameters of therapeutic effect [7,8]. In cervical dystonia, according to one study, Dysport was found to be more effective but resulted in more adverse effects compared with Botox [9].

In our study, patients with hemifacial spasm and blepharospasm who had experienced primary or secondary therapy failure with Botox showed a beneficial response to Dysport administration, except for one patient with tardive blepharospasm who did not respond to either drug.

The reasons for primary or secondary therapy failure with botulinum toxin are numerous. The most common cause of primary therapy failure is misdiagnosis of blepharospasm as congenital ptosis or apraxia of eyelid opening. Also, some subtypes of focal dystonia, such as dystonic tremor or sensory blepharospasm, are known to be less sensitive to botulinum toxin [2]. Pre-existing botulinum toxin antibodies or cross-reactions of botulinum toxin with other antibodies, such as tetanus antitoxin, are also suggested as causes of primary therapy failure [10].

Secondary therapy failure of botulinum toxin treatment can be the result of exacerbations of blepharospasm or hemifacial spasm, or patient's stress and depression [2]. Antibodies that block or neutralize botulinum toxin are suggested as the main cause of secondary treatment failure [12-14]. This serotype-specific antibody response was found in 5% of patients with cervical dystonia treated with Botox after 2–3 years of botulinum toxin and was associated with high dosage and high treatment frequency [11,15]. Since both Dysport and Botox are botulinum type A neurotoxins with presumably similar immunological properties [16], it is not clear why Dysport was effective in cases of secondary Botox therapy failure.

Intracellular mechanisms are also involved in botulinum toxin activity. The endopeptidase cellular activity of botulinum toxin light chain, which specifically cleaves SNARE (soluble N-ethylmaleimide-sensitive factor-attachment protein-receptor) proteins, results in inhibition of the cascade preceding neurotransmitter release [17-19]. It has been shown that the light chain enzymatic activity is also responsible for prolonged duration of action of the neurotoxin. This activity is serotype specific and changes over time [20]. Consequently, the intracellular accumulation of botulinum toxin light chain could be another putative mechanism responsible for the differential activity of various botulinum toxin preparations.

Unlike previous reports that found no clear difference between the therapeutic effect of Botox and Dysport [7-9], we suggest, based on our findings, that a shift from one product to another should be considered in case of primary, or secondary, failure with one product.

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**Correspondence:** Dr. S. Badarny, Dept. of Neurology, Carmel Medical Center, Haifa 34362, Israel.
Phone: (972-4) 825-0390
Fax: (972-4) 825-0693
email: samihba@clalit.org.il


## *Capsule*

### Body piercing in England

In their study on body piercing, Bone and co-authors investigated its prevalence, other than of earlobes, in the general adult population in England, as well the distribution of this practice by age group, gender, social class, anatomic site, and who performed the piercings. They also estimated the proportion of piercings that resulted in complications and the proportion of piercings that resulted in professional help being sought after the piercing. The population studied comprised 10,503 adults aged 16 and over selected by a two-stage process: random selection of geographic areas and filling predefined quotas of individuals. Results were weighted to reflect the national demographic profile of adults aged 16 and over. The prevalence of body piercing was 1049/10,503 (10%). Body piercing was more common in women than in men and in younger age groups. Nearly half the women aged 16–24 reported having had a piercing (305/659, 46.2%). Of the 754 piercings in those aged 16–24, complications were reported in 233 (31.0%, 26.8–35.5%); professional help was sought for 115 (15.2%), and hospital admission was required for 7 (0.9%). The authors conclude that body piercing is common in adults in England, particularly in young women. Problems are common and the assistance of health services is often required. Though serious complications requiring admission to hospital seem uncommon, the popularity of the practice might place a substantial burden on health services.

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Eitan Israeli