

## Combination of Botulinum Toxin type A and Hyaluronic Acid Filler for Treatment of Moderate to Severe Glabellar Rhytides: results of one year follow up

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**Abstract: Introduction:** Prominent glabellar wrinkles are unpleasant facial stigmata. A number of procedures is used for management. The Plastic surgeons frequently administer botulinum toxin A or hyaluronic Acid Filler as monotherapy to treat glabellar rhytides. **Objectives:** To evaluate the possible advantages and disadvantages of combination therapy; (botulinum toxin type A and hyaluronic Acid Filler) for treatment of moderate to severe glabellar rhytides. **Patients and methods:** 60 cases, 40 women and 20 men, were treated in the period from January to October 2012. All cases had at least visible glabellar rhytides at rest that deepen at maximum frown with age between 22 to 60 years. Treatment was done by injection of botulinum toxin type A of glabellar muscle complex followed by injection of hyaluronic acid filler in the same session. We used a photonic guide to grade the severity of the patient's glabellar lines at baseline both at rest and at maximum frown as well as patient's self-perception of age. Assessment was performed at days 10, 90, 180 and 360. We and patients reported the global assessment of change in glabellar line severity (complete improvement, improvement, unchanged, worse condition). Also, patients were asked to assess the change in their self-perception of age and the need for repeated injection. **Results:** Overall, cases had a positive self-image at baseline, irrespective of worrying about glabellar lines in 53 cases and complain of appearing stressed in 6 cases and appearing tired in 1 case. At day 10 and 90, we reported that all the cases (100%) had complete improvement in glabellar line severity. At days 180 and 360, 95% (57 cases) and 80% (48 cases) of cases, respectively reported satisfaction with various aspects of the effects of treatment (time to onset of action, improvement in glabellar lines and appearance, and appearing better) and the procedure itself (absence of downtime and side effects). all cases considered that they looked younger than they did before treatment. 3 cases required repeated injection after 180days and 12 cases required repeated injection after 360days. **Conclusion:** Botulinum toxin type A administration is successfully combined with hyaluronic acid filler therapy. They provide optimal treatment of moderate to severe glabellar rhytides and enhance treatment outcomes. Patient satisfaction further highlighted the superiority of the combination approach. Patients thought they appeared younger than they did before treatment. The combination therapy has decreased the need for repeated injection of Botulinum toxin.

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**Key Words:** botulinum toxin, hyaluronic acid filler, glabellar rhytides, upper face rejuvenation

### 1. Introduction:

Facial rhytides are often unwelcome either because they are signs of aging or because they can be misinterpreted and mistakenly perceived to signify stress, anxiety, annoyance, disapproval, or anger [1, 2].

The presence of facial rhytides can have a negative impact on patients' perception of themselves and also on other people's impressions of them. As a result, they may seek treatment to achieve a more youthful appearance, to help them appear their best, to prevent miscues of facial communication, or simply to feel better about their appearance [1,2].

Glabellar Lines, Sometimes called the 'Eleven', are those vertical lines that develop between the eyebrows as a result of frowning, scowling, or merely focusing while listening or reading. Sometimes bad eyesight or insufficient

corrective lenses can contribute to the muscle contractions that deepen the glabellar lines [3, 4].

Like other creases, wrinkles and lines on the face, glabellar Lines are now easily treated with Botulinum Toxin alone or with dermal fillers alone or in combination. Common question about combination therapy is how to approach the practical application of each treatment [5]. Before doing these procedures, the doctor should have a thorough knowledge of the facial anatomy and location of the underlying neurovascular structure.

We use the combination therapy of Botulinum Toxin type A (BTX A) and Hyaluronic acid filler (HA) at the same time for treatment of moderate to severe glabellar rhytides. This approach can optimize the result of both agents. The dermal filler can camouflage the recovery of muscles from

the Botulinum Toxin effect thus decreasing the need for reinjection.

The scope of this article is to present our approach in management of glabellar rhytids combination therapy BTX A and HA. Also, to present the results of one year follow up of a series of 60 cases treated by this approach including advantages, disadvantages and the need for further treatment.

## 2. Patients and methods

This study included 60 cases, 40 women and 20 men, treated in the period from January to October 2012. All cases had at least visible glabellar rhytides at rest that deepen at maximum frown with age between 22 to 60 years. All cases were required to sign informed consent for these treatments.

### 2.1 Baseline Assessments

We used a photonic guide to grade the severity of the patients' glabellar lines at baseline, pretreatment, both at rest and at maximum frown. Cases in this study had at least visible glabellar rhytides at rest that deepen at maximum frown. We assessed also patients' self-perception as appearing tired, stressed, or worrying about facial lines, and patient self-perception of age.

### 2.2 Exclusion Criteria

Patients were excluded from the study if they had facial aesthetic surgery in the preceding year; had a significant facial movement disorder or preexisting brow or eyelid ptosis. We also excluded patients with history of cerebrovascular accident, head injury, or other cerebral damage affecting the recognition or expression of emotion; any psychiatric illness that might interfere with the ability to produce facial expressions or experience emotion normally; any disorder or were using any agent that might interfere with neuromuscular function.

Pregnant and breastfeeding women and those with a childbearing potential and not using reliable contraception were also excluded.

### 2.3 Treatment Regimen

In all cases BTX A was injected firstly; Reconstitution of BTX A was performed immediately before injection using non preserved injectable saline. All injections were administered by a single investigator. We use 20 to 40 units of BTX A (divided injections in corrugator and procerus muscles) by 5- injection site pattern at the glabellar wrinkles, and 20 to 40 units of BTX A (divided injections in frontal muscle) by 2- row of injection site pattern using a 30-gauge needle. This is followed by injection of hyaluronic acid filler 25 mg/ml. usually half ml enough to treat the vertical glabellar rhytides in same session.

## 2.4 Efficacy Outcome Measures

At days 10, 90, 180 and 360: we and patients reported the global assessment of change in glabellar line severity (complete improvement, slight improvement, unchanged, worse condition)

We considered the change in glabellar line severity at both rest and maximum frown when determining the global level of improvement and used preinjection baseline photography (at both rest and maximum frown) to assist the evaluation. Also patients were asked to report whether they thought they appeared younger, the same age, or older compared with before treatment.

## 3. Results

### 3.1 Patients treated

A total of 60 cases, 40 women and 20 men, received treatment and all patients completed the study. All cases in this study had at least visible glabellar rhytides at rest and become deepen at maximum frown. Overall, cases had a positive self-image at baseline. Irrespective of worrying about glabellar lines in 53 cases, complain of appearing stressed in 6 cases and appearing tired in 1 case

### 3.2 Efficacy

#### 3.2.1 Global Assessment of Change in Glabellar Line Severity:

At day 10 and 90 we reported that all the cases (100%) had complete improvement in glabellar line severity from baseline. while these percentage changed at days 180 and 360, 95% (57 cases) and 80% (48 cases) of patients, respectively (Figures 1-4).

#### 3.2.2 Patients' Self-Perception of Age;

At day 10 and 90 the cases reporting that they appeared younger after treatment by the 100 %. These patients perceived that they appeared younger by at least of 5 years. No patient thought they appeared older after treatment. At day 180, 5% (3 cases) retained to near base line and this percentage increased to become 20% (12 cases) at day 360; and required repeated injection.

#### 3.2.3 Patient Satisfaction and Tolerability;

All the patients reported primary satisfaction with various aspects of the effects of treatment (time to onset of action, improvement in glabellar lines and appearing better) and the procedure itself (minimal side effects and absence of downtime).

Adverse events that were considered probably or definitely related to treatment were limited to feeling pressure (reported in 12 percent of patients), soreness/itching at the injection site (5 percent), and headache (2 percent). None was serious and all were self limiting and mild except for a moderate headache in one patient.



**Figure 1: A 50 years old female pre-injection (right) and 180 days post-injection**



**Figure 2: A 38 years old male pre-injection (right) and 180 days post-injection**



**Figure 3: A 42 years old male pre-injection (right) and 360 days post-injection**



**Figure 4: A 53 years old male pre-injection (right) and 360 days post-injection showing partial recurrence of vertical glabellar rhytides**

#### 4. Discussion:

Facial aging changes occur as the result of a number of factors, including external environmental impacts, muscle action, and genetics. Most patients present for the treatment of visible lines, wrinkles, and folds. The etiology of the rhytides must be established for appropriate treatment. Dynamic rhytides are caused by muscle action and are seen during facial animation (e.g. smiling, talking, and frowning). Static rhytides are visible at rest, although they may deepen during animation. Over time, untreated dynamic rhytides may form static rhytides. However, the formation of static rhytides is influenced by additional factors, such as photodamage and loss of skin elasticity. [6]

The clinician must ascertain the physiologic basis of the observed changes to create an appropriate treatment plan. For example, dynamic wrinkles associated with muscle action are best approached with BTX-A. Conversely; folds caused by the loss of subcutaneous fat will not respond effectively to BTX A and must be corrected with soft-tissue augmentation or possibly surgical intervention. [5]

A number of studies as well as clinical experience have supported the efficacy of combining treatment modalities for optimal results. Dermal fillers, BTX A, light/energy therapy, and chemical resurfacing are common modalities that have been combined successfully in aesthetic treatment plans. [3-7]

We used the combination therapy of BTX A and HA at the same time for treatment of moderate to severe glabellar rhytides to presents the experience with this combination therapy together with indications, techniques, and complications associated of this combination therapy in rejuvenation of glabellar rhytides.

Cases in this study have at least visible glabellar rhytides at rest that deepen at maximum frown.

BTX A has been used for numerous medical conditions worldwide. Clinical trials assessing the efficacy of aesthetic use of BTX A showed a response rate of approximately 80% with response starting to fade at about 90 days. [8, 9]

Clinicians need a complete understanding of facial anatomy in order to optimize results with BTX A therapy and to avoid complications. The most commonly treated muscles in the upper face are the muscles of the glabellar complex: the corrugator supercilii, procerus, and depressor supercilii [10].

Contraction of the corrugator supercilii muscle draws the eyebrows centrally and inferiorly, contributing to the formation of vertical and oblique lines ("frown lines") in the glabellar area [11]. The

procerus depresses the medial portion of the eyebrow, contributing to the formation of transverse glabellar lines. The depressor supercilii muscle also depresses the medial portion of the eyebrow and thus contributes to the formation of transverse glabellar lines [11, 12].

In all cases BTX A was injected firstly; Reconstitution of BTX A was performed immediately before injection using non preserved injectable saline. We used 20 to 40 units of BTX A (divided injections in corrugator and procerus muscles) by 5- injection site pattern at the glabellar wrinkles, using a 30-gauge needle.

Beyond the glabellar complex, 2 additional upper-face muscles are commonly approached for treatment with BTX -A with very satisfying results: the frontalis and the orbicularis oculi.

The frontalis is the one true elevator muscle in the upper face, serving to raise the eyebrows. Repeated contraction of the muscle causes horizontal forehead lines. The actions of the orbicularis oculi muscle contribute in different ways to the formation of lines in the periocular region [10, 11].

Macdonald and colleagues [12] identified gender differences in upper-face musculature following their dissection of 50 cadaver hemibrows (24 males, 26 females). These gender-based anatomical differences provide a clear indication that clinicians should treat according to the patient's individual anatomy in order to achieve good results.

A solid understanding of facial anatomy, coupled with proper treatment dosing, helps to prevent treatment complications resulting from the migration of toxin into unintended areas. Once they have occurred, these complications will typically fade after several weeks. [11, 12] these clarify why the dose changed between the 20 to 40 IU among the cases. Clinicians should consider their individual experience; patient anatomy, gender, and goals; and the pattern, mass, and activity of the muscles to be treated to select and refine doses for specific treatments.

We inject HA fillers at the glabellar furrow after BTX A injection at the same session to elevate the furrow and restore volume thus, giving more satisfaction in our cases.

Dermal-filler injections are a well-established first-line approach to treating volume loss, with BTX A, resurfacing, and other modalities serving as complementary adjunctive therapies. [5]

The use of soft-tissue fillers in cosmetic enhancement dates back over 100 years. Collagen was the most commonly used dermal filler until the 2003 FDA approval of injectable HA fillers for aesthetic use [14]. HA fillers have since been adopted

by many clinicians as the first-choice products for soft-tissue augmentation, and as a class they currently represent the third most popular cosmetic procedure overall [13].

From our results; we reported that all the cases (100%) had complete improvement in glabellar line severity from baseline and all cases (100%) felt that they appear younger after treatment at days 10 and 90. while this percentage changed at days 180 and 360; becoming 95% (57 cases) and 80% (48 cases) of patients, respectively. this indicates optimal results of combination therapy in treating the glabellar rhytides than one of them alone.

At days 180, 5% (3 cases) retained to near base line and this percentage increase to become 20% (12 cases) at days 360. These cases required repeated injection of BTX A.

The use of BTX A is the usual treatment of choice in management of glabellar rhytids as the use of fillers alone doesn't produce the desirable rejuvenating effect. This is attributed to the strong influence of glabellar complex muscles on the skin [10]. The results of this study suggest that simultaneous use of HA filler with BTX-A achieve better esthetic results in moderate to severe cases.

After 6 months follow up, only 5% of patients needed reinjection compared to a 100% rate of reinjection needed with the use of BTX A alone [8]. This can be explained by that the use of HA filler camouflaged the recovery of muscles from the effect of BTX-A. With the follow up period extended to 1 year, we found that only 20% of cases retained to near base line. This may be explained by the effect of BTX-A on the delay of absorption of HA due to stasis of the area of injection in the early months after treatment.

The versatility of our approach is highlighted by the fact that all patients reported primary satisfaction with various aspects of the effects of treatment and the procedure itself.

We found this combination to be safe with no extra adverse effects related to combining both agents. Adverse events that were considered probably or definitely related to treatment were limited to feeling pressure (reported in 12 percent of patients), soreness/itching at the injection site (5 percent), and headache (2 percent). This incidence of side effect is no significantly different from using one agent alone [10, 14].

## Conclusion

Botulinum toxin type A administration is successfully combined with hyaluronic acid filler therapy and can be injected at same session. Patient satisfaction further highlighted the superiority of the

combination approach. Dual therapies provide optimal treatment and enhance treatment outcomes of glabellar rhytides. Also decrease requirement for repeated injection of Botulinum toxin type A. Optimal outcomes in glabellar rhytides however; require in-depth knowledge of facial aging and anatomy, an appreciation that rejuvenation is a three-dimensional process involving muscle control, volume restoration, and recontouring.

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