

Combined Non-Surgical Therapy for Facial Rejuvenation with “Botulinum Toxin Type A” and Injectable Fillers

ALAA EL-DIN AM EL-MOGHAZY, M.D.

The Department of Plastic & Reconstructive Surgery and Burn Unit, Faculty of Medicine, El-Minia University.

ABSTRACT

Non-surgical treatment of facial aging can be described from various perspectives by the nature of the deformity, by the skin layer in which the pathology occurs, or by the technique used to address it. Because of the many causes of rhytids, in as much as various anatomic locations that respond differently to treatment and over time the effects of aging coincide and overlap and so, the optimal treatment often necessitates a multifaceted approach. It is believed that when Botulinum toxin type-A (BTX-A) is used in combination with hyaluronic acid fillers in the appropriate patient in the same region, it reduces the muscular movement of the face, which allows for greater tissue residence of the filler and restoration of the balance of facial movement and position.

Aim: The aim of this study was to review and describe our experience with combination therapy for facial skin rejuvenation using butulinum toxin type-A (BTX-A) injections with dermal fillers most commonly used in our practice, namely hyaluronic acid derivatives (Restylane, Juvederm), Polyacrylamide hydrogel (Esteform), or combination (Amazingel).

INTRODUCTION

Because of the many causes of facial changes, inasmuch as various anatomic locations that respond differently to treatment and over time, the effects of aging coincide and overlap and so, the optimal treatment often necessitates a multifaceted approach [1,2]. The traditional concepts of soft-tissue descent associated with aging (for which the lift was the solution) have been supplemented with the reality that the illusion of descent is often a manifestation of regional volume depletion [3].

Non-surgical treatment of facial aging can be described from various perspectives by the nature of the deformity (wrinkle, fold, or furrow), by the skin layer in which the pathology occurs (epidermis or dermis), or by the technique used to address it (exfoliation, injectables, resurfacing, or chemodenervation) [4]. Office-based non-surgical facial rejuvenation is done by one of the following methods: Butulinum toxin type A (BTX-A) for chemodenervation of the muscle contributing to

the dynamic lines; [1,2,5] Lasers, chemical peels, or dermabrasion for resurfacing of the static lines; [6] and the injectable fillers to replace missing dermal components or subcutaneous fat (volumetric restoration) [3]. The cosmeceutical topical agents can also be a useful complement and supplement non-surgical techniques.

Although injectable agents for soft tissue augmentation have been widely available for more than 20 years, the renewed interest has been fueled in part by the introduction of BTX-A [3]. It is a powerful agent that specifically and physiologically denervates the mimetic muscles that cause facial changes associated with aging face due to underlying muscular activity, muscle hypertrophy and facial expression by relaxation or altering the balance between agonist and antagonist of facial muscles. Now, BTX-A therapy has evolved from just a "wrinkle treatment" to a method of "facial reshaping" [5].

It is believed that when BTX-A is used in combination with hyaluronic acid fillers in the appropriate patient, it can restore facial appearance by the dual mechanisms of reflation and relaxation [7]. BTX-A reduces the muscular movement of the face, which allows for greater tissue residence of the filler and restoration of the balance of facial movement and position. This appears to increase the longevity of tissue dwell time of the filling agent [3,5,7]. Chemical peel can also be used in conjunction with BTX-A and dermal fillers with synergistic beneficial effect, but surprisingly, descriptions of such combinations are rare in the current medical literature [6].

PATIENTS AND METHODS

A total number of 31 patients, aged between 24 and 50 years, who came to our clinic for cosmetic treatment and facial rejuvenation using both

BTX-A and an appropriate filler, in the period from September, 2006, to July, 2008, were enrolled in this study. They were assessed clinically and photographically to follow-up the facial skin and appearance improvement.

Subjects with facial wrinkles, contour deformities or soft tissue deficiencies caused by aging were included. Patients presented with uncontrolled diabetes mellitus, known drug allergy, pregnancy, lactation, acute inflammatory disease, connective tissue disorders, skin disorders, compromised immune functions, or mental disorders were excluded from this study. Data were collected, tabulated, discussed and evaluated. They were injected with BTX-A and appropriate filler (Restylane, Perlane, Juvederm, Esteform and Amazingel) in the same session with BTX-A being injected first or in two different sessions with BTX-A being injected at the first session, or in the second session after an interval of one to two weeks in between.

After facial cleansing with appropriate antiseptic agent, topical anesthetic cream (EMLA) was used on the areas to be injected with BTX-A for 30-45 minutes with or without occlusive dressing. For injectable fillers, local anesthesia infiltration at site of port entry of the injection needle with 0.5ml of "Xylocain" 1% was done. After finishing injection, the site of port entry of the injection needle was dressed with a small piece of "Steri-strip" tape. Patients were advised not to touch the face for next 24 hours and avoid sleeping on their faces. But on the other hand, they were encouraged to do some facial expressions to exhaust facial muscles. After 24 hours, they can wash their faces gently.

Next follow-up session for revision was after 7-14 days, except if some bruises or ecchymosis appeared, they were advised to use a topical vitamin K oxide ointment with gentle massage, tangentially and upwards. Photographs were taken before injection and at follow-up visits.

BTX-A (Allergan Pharmaceuticals Inc, Irvine, California, USA) was diluted with 2ml of 0.9% normal saline (0.02ml contains 1 unit of toxin), just before injection. The rest of the bottle was kept refrigerated until the revision session for maximum 2 weeks. The initial dose ranged from 44-72 units according to the area of injection, exaggeration of expression and age and gender of the patient. In the revision, the dose ranged between 20-40 units.

Restylane (Q-Med Co., Sweden) was used for superficial wrinkles, nasolabial fold, lip contouring

or augmentation, or on top of Perlane injection for folds. Perlane (Q-Med Co., Sweden) was used for nasolabial fold or malar augmentation. Juvederm (Allergan, Pharmaceuticals Inc., Irvine, California, USA) was used for superficial wrinkles, nasolabial fold, or lip contouring and augmentation. Esteform (Safe Fill Co. Ltd, Ukraine) was used for cheek, malar, or chin augmentation. Amazingel (Merrystone Medicine Science and Technology Development Co. Ltd, China) was used for cheek, malar, chin augmentation and around lateral orbital wall. The amount of injectable material ranged between 1-10ml according to the area to be treated. The revision dose ranged between 1-4ml.

RESULTS

A total number of 31 patients, aged between 24 and 50 years, with a mean age of 29.6 ± 8.7 years, who came to our clinic for cosmetic treatment and facial rejuvenation using both BTX-A and an appropriate filler, in the period from September, 2006, to July, 2008. Twenty-three were females (74.19%) and 8 were males (25.80%) (Table 1). Our demographic data is represented in (Table 2). Follow-up period ranged from 1 month to 12 months. Two patients were lost in the follow-up (both were females).

Patients were injected with BTX-A and appropriate filler (Restylane, Perlane, Juvederm, Estiform and Amazingel) in the same session with BTX-A being injected first (Table 3) or in two different sessions with BTX-A being injected at the first session (Table 4), or in the second session after an interval of one to two weeks in between (Table 5). All the patients tolerated the procedure well, except for one female that suffered from intense pain with injection which resolved after few minutes with cold compresses.

Adverse events that could be ascribed to the treatment were observed in 8 cases (25.82%). They were most commonly presenting as transient erythema or edema in 3 cases (09.70%), that resolved spontaneously, or a hematoma formation in 2 cases (06.45%), that resolved spontaneously or after message with vitamin K oxide cream. In another case (03.23%), a slight change of skin color at the site of injection was observed. Also, two patients (06.45%) had developed visible mucosal lip nodules, but no one required intervention (Table 6).

The best aesthetic result (confirmed by another physician and the patient) was in the group treated with the filler in a second session after BTX-A has been administered at a previous session.

Table (1): Sex distribution of cases injected with Botulinum toxin type A and filler.

| | BTX-A injected before filler injection | BTX-A injected with the filler at same session | BTX-A injected after filler by 1-2 weeks | Total |
|--------------|--|--|--|-----------|
| Females | 9 | 7 | 7 | 23 |
| Males | 1 | 5 | 2 | 8 |
| Total | 10 | 12 | 9 | 31 |

Table (2): Demographic data.

| Number of cases | Sex | Age | Botulinum Toxin Type A (BTX-A) | | | Fillers | | | | Time of injection of Botulinum toxin type A | | |
|-----------------|-----|-----|--------------------------------|-----------------------------|----------------------------|----------|------|-------------------------------|------------------------------|---|--------|-------|
| | | | Site | Total dose first session ml | Total dose for revision ml | Site | Type | Total amount first session ml | Total amount for revision ml | Same | Before | After |
| 1 | F | 45 | al L Cl rn | 44 | 30 | Ma L | J | 2 | 1 | - | ++ | - |
| 2 | F | 24 | Cr Ll | 50 | 22 | Ma Ck | E | 7 | 2 | - | - | ++ |
| 3 | F | 24 | Cm Cr Ll | 46 | 24 | Ma Ck Ch | E | 4 | 2 | ++ | - | - |
| 4 | F | 41 | Fr Gl Cr | 52 | 22 | Cr Fr | R | 1 | - | - | ++ | - |
| 5 | F | 30 | Cv | 60 | 24 | Cv | A | 2 | 1 | ++ | - | - |
| 6 | F | 24 | Ph L Cl | 54 | 28 | Ph L | R | 1 | - | - | - | ++ |
| 7 | M | 50 | Cm Cv Ll | 72 | 25 | Ch Ma Cr | E | 6 | - | ++ | - | - |
| 8 | M | 34 | Ll Rn Cl | 68 | 26 | Nl | R | 2 | - | - | ++ | - |
| 9 | F | 27 | Fr Gl Ll | 50 | 25 | Fr Ck Lo | A | 4 | 2 | - | ++ | - |
| 10 | F | 41 | Cr Ll Cm | 48 | 30 | Cr L | R | 1 | - | ++ | - | - |
| 11 | F | 37 | Cr Ll al | 52 | 20 | Ma Ck Lo | A | 8 | - | - | ++ | - |
| 12 | M | 49 | Cm Ll | 70 | 20 | Nl | R | 2 | - | ++ | - | - |
| 13 | F | 31 | Ph Cl L | 62 | 21 | Ch L | J | 4 | - | - | - | ++ |
| 14 | F | 45 | Gl Cl al | 60 | 24 | Nl Gl | P | 2 | - | - | ++ | - |
| 15 | M | 48 | Fr Gl Br | 66 | 28 | Gl | R | 1.6 | - | ++ | - | - |
| 16 | F | 34 | Fr Gl Rn | 68 | 26 | Gl | R | 2 | - | - | - | ++ |
| 17 | F | 27 | al Cl L | 50 | 25 | Ph Ma | A | 4 | 1 | - | - | ++ |
| 18 | F | 41 | Cl L | 48 | 30 | L | J | 1 | - | - | - | ++ |
| 19 | F | 37 | Cl L Cv | 52 | 20 | Cv L | J | 1 | - | - | ++ | - |
| 20 | F | 42 | Cr Ll rn | 58 | 20 | Ma Ck Lo | E | 2 | 1 | - | ++ | - |
| 21 | F | 43 | Cv Ll Rn | 55 | 27 | Ma Cv | A | 4 | - | - | - | ++ |
| 22 | F | 40 | Fr Gl Ll | 48 | 22 | Gl Ma | R | 3 | 1 | - | ++ | - |
| 23 | M | 50 | Rn al Cl | 56 | 30 | Nl | J | 1 | - | ++ | - | - |
| 24 | F | 50 | Cm Cl al | 54 | 20 | Ph L | R | 1 | - | ++ | - | - |
| 25 | M | 47 | Cm Cl L | 70 | 20 | Gl Fr Cr | E | 1 | - | - | - | ++ |
| 26 | F | 24 | Cr Ll Cm | 54 | 28 | Nl Ck Lo | P-A | 1-2 | 0-1 | ++ | - | - |
| 27 | M | 50 | Cm Cl al | 72 | 25 | Nl L | J | 2 | 1 | ++ | - | - |
| 28 | F | 49 | Cm L | 70 | 20 | L | R | 2 | - | ++ | - | - |
| 29 | F | 31 | Ll rn al ph | 62 | 22 | Ph Ma Ck | E | 4 | 1 | - | ++ | - |
| 30 | M | 45 | Cv Rn al | 60 | 24 | Nl Cv | P | 2 | - | - | - | ++ |
| 31 | F | 48 | Cv Ll Cm | 68 | 28 | Nl Cv | P | 1.4 | - | ++ | - | - |

F : Female. Br : Brow. Cl : Columella. Ch : Chin. Ch: Cheek. R: Restylane.
M: Male. LL: Lower lid. al : Ala. L : Lip. Lo: Lateral orbital depression. P: Perlane.
Gl: Glabella. Cr : Crow's feet. Cm: Corner of mouth. Nl : Nasolabial fold. Cv: Cervical rhytids. A: Amazingel.
Fr: Forehead. Rn: Root of nose. Ph : Peri-mental hollow. Ma: Mala. J : Juviderm. E: Esteform.

Table (3): Cases injected with Botulinum toxin type A and the fillers at same session.

| | |
|---------------------|-----------|
| Restylane | 5 |
| Juviderm | 2 |
| Perlane (Restylane) | 2 |
| Amazingel | 2 |
| Esteform | 2 |
| Total | 12 |

Table (4): Cases injected with Botulinum toxin type A before filler injection.

| | |
|---------------------|-----------|
| Restylane | 3 |
| Juviderm | 2 |
| Perlane (Restylane) | 1 |
| Amazingel | 2 |
| Esteform | 2 |
| Total | 10 |

Table (5): Cases injected with Botulinum toxin type A after fillers by 1- 2 weeks.

| | |
|---------------------|----------|
| Restylane | 2 |
| Juviderm | 2 |
| Perlane (Restylane) | 1 |
| Amazingel | 2 |
| Esteform | 2 |
| Total | 9 |

Table (6): Adverse effects.

| Adverse effect | Number of cases | Percentage |
|-----------------------|-----------------|--------------|
| Erythema and/or edema | 3 | 09.70 |
| Hematoma | 2 | 06.45 |
| Skin coloration | 1 | 03.23 |
| Lip mucosal nodule | 2 | 06.45 |
| Total | 8 | 25.82 |

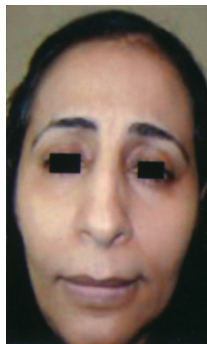


Fig. (1-A): Pre-injection view of glabellar furrow injected with BTX-A at first session.



Fig. (1-B): Post-injection view of the glabellar furrow after Perlane injection (two weeks).



Fig. (2-A): Pre-injection view of pre-orbital depression. BTX-A was injected at Crow's feet and inferior lid.



Fig. (2-B): Post-injection view of Amazingel injection at lateral orbital depression, Mala and cheek after 2 weeks.



Fig. (3-A): Pre-injection view of pre-mental depression.



Fig. (3-B): Post-injection view after injection of Mala, inferior angle of the mouth and pre-mental depression with Esteform.



Fig. (4-A): Pre-injection view of pre-mental depression.



Fig. (4-B): Post-injection view after injection of pre-mental depression with Esteform.

DISCUSSION

With advances in the availability of newer filling agents and a better understanding of the clinical esthetic effect of botulinum toxin type A (BTX-A), remarkably sophisticated and refined results can now be achieved by using both modalities. This is mostly due to the great appreciation and understanding by the cosmetic physician that the three dimensional aspects of the face must be preserved or replaced to achieve an optimum aesthetically pleasing results [3,8].

BTX-A injection and filler agents are the most popular aesthetic procedures performed [4,5]. BTX-A is used primarily for upper third of the face and neck, while the fillers for the mid and lower face [8]. BTX-A can be used now in another areas of the face; the orbicularis oris, mentalis and depressor anguli oris, with improvement of overall facial appearance [5].

A combination of both BTX-A and fillers has taken on many forms [3]. They may be applied to independent facial regions, or in the same region. It is believed that when both BTX-A and fillers are used in combination in the appropriate patient in the same region, the result is a fuller, smoother, with more youthful appearance [4]. The synergistic effects, however, of combining both agents in the same region where this may be appropriate is appreciated. BTX-A reduces the muscular movement of the face, which allows for greater tissue residence of the filler agents and restoration of the balance of facial movement and position [3,5-7].

Facial regions that more obviously benefit from combination treatment are those areas that have transitioned from dynamic to static lines, furrows, and depressions (as glabellar furrows that are present at animation and at rest and the "down-turned" corners of the mouth). Using BTX-A alone in these situations has only a modest effect, as the surface contour changes are present even with complete chemodenervation and then, fillers are indicated [3]. Correcting wrinkles is now done by restoring volume and relaxing the pull of the muscles that creates negative facial expressions such as glabellar folds, mouth furrows, Crow's feet, horizontal forehead lines and cervical rhytids [7]. Furthermore, as the volume loss is more commonly associated with areas of greater movement (animation), it has been well demonstrated that longer lasting effects with injectable fillers can be achieved with the concomitant use of BTX-A, which also decreases dissipation of the implant. Such regions

include the brow, lips, chin and perimental hollows [3,5-7]. In this study, the areas that had the best results were the glabella (Fig. 1A,B), lateral orbital depression (Fig. 2A,B), cervical rhytids and perimental depressions (Figs. 3A,B,4A,B).

Some authors perform a comprehensive aesthetic evaluation for the assessment of the treatment required whether BTX-A, a filler agent, or both [3]. He injects the appropriate amount of local or regional anesthesia to the treatment area followed by injection of the filling agent and lastly the BTX-A, claiming that this allows for maximum comfort for patient and physician, and the ability to provide both treatments at the same setting and provides for more accurate destination for the toxin [3].

In this study, as regard BTX-A dose, men required more units of toxin than women and that may be related to muscle activity and bulk (Table 2). Treatment of the forehead was being accomplished by fewer units of toxin. This helped to preserve the natural look of some movement of the forehead [5]. Most females asked for BTX-A to be injected at different session (either before or after) (16/23), But most of the men had the injection at the same session (5/8). The most common filler used was Restylane (Perlane) (10+4/31) while Juvederm, Esteform and Amazingel were 6 cases each.

In this study, it was obvious that injection of the filler at the same time with the toxin is beneficial to the patient. He had both treatments at the same session with almost pain free environment. But for the physician, the toxin is better to be administered first, in the same session or in a previous one, to get the proper amount in the proper site. Injection of the toxin in a second session, after the filler, was somewhat difficult, especially after injection of Polyacrylamide gel. The best esthetic results we got were with the cases that treated with the BTX-A in a previous session and then the filler in another session (about 2 weeks before).

We noticed that post-injection massage of fillers frequently resulted in a decreased final correction and needs to be done gently because of the forceful displacement of the material deep both peripherally and into the subcutaneous space.

It is obvious that this study is considered as a preliminary one, and another study on larger scale should be done for each type of filler at each specific area of the face, which is currently going on.

Conclusion:

Non-surgical facial rejuvenation can be achieved by injectable soft tissue augmentation with different types of fillers and also, by chemodenervation with BTX-A, used both independently or in combination for the most comprehensive results.

When combined in the same area, the best results are with the cases that treated with the BTX-A in a previous session (about 2 weeks before).

Ultimately, we must rely on both real science and clinical experience to offer particular agents among the options available to our patients.

REFERENCES

- 1- Carruthers J.D., Lowe N.J., Menter M.A., Gibson J. and Eadie N.: Double-blind, placebo-controlled study of the safety and efficacy of Botulinum toxin type A for patients with glabellar lines. *Plast. Reconstr. Surg.*, 112: 215; 2003.
- 2- Spiegl J.H.: Treatment of peri-orbital rhytids with Botulinum toxin type A: Maximizing safety and results. *Arch. Facial Plast. Surg.*, 7: 198, 2005.
- 3- Klein A.W. and Fagien S.: Hyaluronic acid fillers and Botulinum toxin type A: Rationale for their individual and combined use for injectable facial rejuvenation. *Plast. Reconstr. Surg.*, 120 (6s): 815, 2007.
- 4- Wise J.B. and Greco T. Injectable treatments for the aging face. *Facial Plast. Surg.*, 22 (2): 140, 2006.
- 5- Flynn T.C.: Update on butulinum toxin. *Semin Cutan Med. Surg.*, 25 (3): 115, 2006.
- 6- Marina L.: Combination of chemical peelings with Botulinum toxin injections and dermal fillers. *J. Cosmet. Dermat.*, 5 (2): 121, 2006.
- 7- Coleman K.R. and Carruthers J.D.: Combination therapy with Botox T.M. and fillers: The new rejuvenation paradigm. *Dermatol. Ther.*, 19 (3): 177, 2006.
- 8- Klein A.W.: Soft tissue augmentation 2006: Filler fantasy. *Dermatol. Ther.*, 19 (3): 129-133; 2006.