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**PERIORAL
RHYTHIDES**
ANATOMY AND TREATMENT

**FACIAL
RESHAPING**
USING AN INTRADERMAL
TECHNIQUE

**MODERN
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**COSMETIC
ENHANCEMENTS**
for the arabic nose

MANAGING LIP RHYTTIDES COMBINING BOTULINUM TOXIN AND HYALURONIC ACID

Alessio Redaelli reviews the results of a study evaluating the use of botulinum toxin and hyaluronic acid to treat perioral rhyttides

ABSTRACT

Background:

The treatment of upper lip wrinkles is often unsatisfactory when using fillers only for the hyperfunctional movement of the orbicularis oris muscle.

Objective:

To evaluate the immediate outcome of the cosmetic use of botulinum toxin A to understand the real rate of side-effects after this part of the technique, and to evaluate the outcome together with hyaluronic acid for the correction of lip wrinkles caused by hyperfunctional movement. It is difficult to correct these wrinkles using just the 'Paris-lip' technique, especially in younger patients.

Materials and method:

In the period from January 2008 until May 2010 the author treated 180 patients: 74 patients were treated with botulinum toxin A alone when 'barcode' wrinkles were the result of hyperfunctional movement of the orbicularis oris (first cohort), and 106 with botulinum toxin A and hyaluronic acid using cannulae when a loss of lip volume was evident over orbicularis oris hypercontraction (second patient cohort).

Results:

Although this is an 'off-label' indication for botulinum toxin use, all patients showed good results, there was not a single case of 'real' side-effects, and no systemic effects were noted. The subjective improvement observed by the patients themselves was also significant.

Conclusions:

Botulinum toxin A is a safe and effective technique in the management of lip wrinkles and can be used as a primary indication. It can also improve the results of filler treatment with immediate and/or long-lasting results. If well performed and explained beforehand, no significant side-effects occur, and any eventual effects are accepted by patients.

FACIAL AGEING IS PRIMARILY THE result of gravity and loss of elastic tissue support owing to subcutaneous changes in the dermis. Consequently, wrinkles are usually strictly linked to age. On the contrary, lip wrinkling often appears in young people as a result of the hyperfunctional movement of the orbicularis oris, as is the case in smokers¹⁻⁴. In these cases, the use of normal fillers alone is insufficient, because it is sometimes impossible to completely eliminate wrinkling during movement of the mouth and, even when possible, the long-term result appears unsatisfactory^{1, 2}. Of the vast range of potentially corrective techniques for these problems (laser resurfacing, peelings, dermal abrasion, revitalisation, implants of re-absorbable and non-resorbable materials, surgical techniques), hyaluronic acid is possibly the most used substance to restore the original lip volume, or for its augmentation in cases of insufficiency^{5, 6}.

In all hyper-mimic patients, the author believes it is possible to use botulinum toxin A with an off-label indication in the initial session. Botulinum toxin has been used for many years and is also used in the lower face, where it is proven to be very safe^{3, 7, 8}. This should prove to be extremely useful in young patients, where the muscular component is more pronounced: in these cases, the single reduction of the muscular contractility is often enough to resolve the problem¹, and the injection of hyaluronic acid will be useful only in cases in which >



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KEYWORDS

botulinum toxin, hyaluronic acid, barcode wrinkles, perioral region, Vistabel, Azzalure



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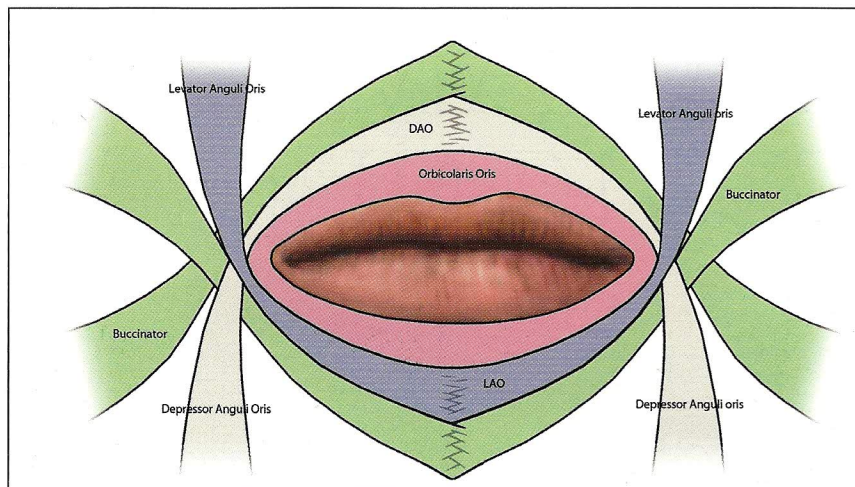


Figure 1 Muscle structures surrounding the mouth

▷ the patients want to improve the volume of the lips. In the older patient, the toxin will improve the aesthetic result but, more importantly, it will extend the duration. In fact, one of the limitations of the resorbable materials in lip treatment is precisely the duration of the result owing to the constant mobility of this region^{2,3,5-7}.

Anatomy

It is important to briefly review the anatomy of the lip, specifically the muscles responsible for forming barcode wrinkles. The orbicularis oris is the sphincter muscle that closes the mouth; it is located very close to the surface, near the mouth's edge (*Figure 1*). It is not a single muscle, but its fibres derive from many other facial muscles. Orbicularis oris fibres are responsible for the barcode wrinkles (red fibres in the *Figure 1*). Then there is a superficial/medium layer, which terminates in the *depressor anguli oris (triangularis)* from the upper lip, and from the lower lip to the *levator anguli oris*⁸. The buccinator muscle lies in a deeper layer; the fibres of the inferior lip derive from the superior part of the buccinator in the cheeks, and those of the superior lip derive from the inferior part of the buccinator at the cheeks. All fibres intersect at the mouth's

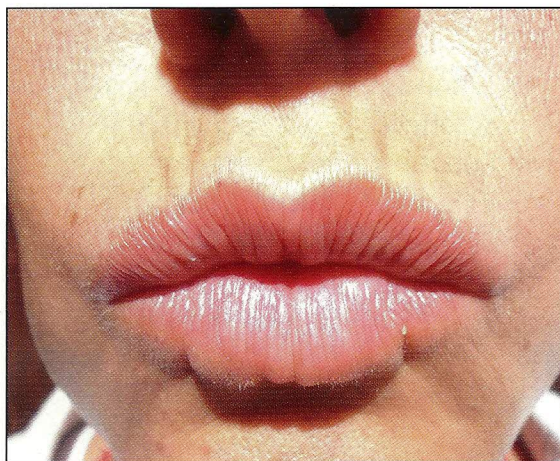


Figure 2 Premature perioral rhytides in a young patient

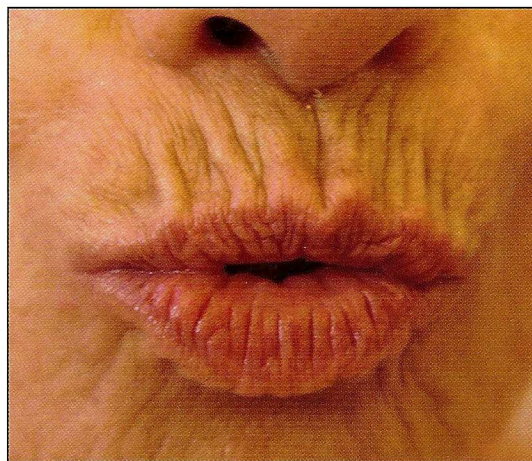


Figure 3 Perioral rhytides in an older patient

commissure. These fibres make up the deep muscle stratum of the lips.

Vertical lip wrinkles

The improvement of radial wrinkles of the lips, close to the mouth edge, is the main goal of treatment. These perioral rhytides appear differently depending on the age of the patient; a premature appearance of these wrinkles is fundamentally a result of hyperactivity of the orbicularis oris (*Figure 2*), often associated with a constitutional lassitude of the same muscle. These 'dynamic wrinkles' appear only during muscular contraction. In these patients, the use of botulinum toxin A is often enough for good results (first patient cohort).

In older people, however, the wrinkles are constantly visible and become more pronounced during lip movements (*Figure 3*). In these patients the orbicularis oris hypermotility is connected with a reduction in lip fullness^{4,8-10} and so, the use of fillers will be indicated.

Materials and methods

In the period from January 2008 until May 2010, the author treated 180 female patients for upper and inferior lip wrinkling. All patients had a hyperfunctional movement of the perioral muscles, with the appearance of barcode wrinkles, and for this very reason were treated with botulinum toxin A. However, 106 patients also showed a reduction of lip fullness and for this reason they were also treated with hyaluronic acid. This resulted in two patient cohorts:

- The first group of 74 (41.2%) patients were treated with botulinum toxin A alone, when only hyperfunctional movement was present without a reduction in lip fullness
- The second group of 106 (58.8%) patients were treated with botulinum toxin A and hyaluronic acid in combination, as over the dynamic component there was also a reduction in lip fullness.

The all-female patient group ranged in age from 30-68 years, with an average age of 43 years. No patients with pregnancy, coagulopathy, or neuromuscular disease were treated^{7,9}. Seven patients were taking ticlopidine ▷

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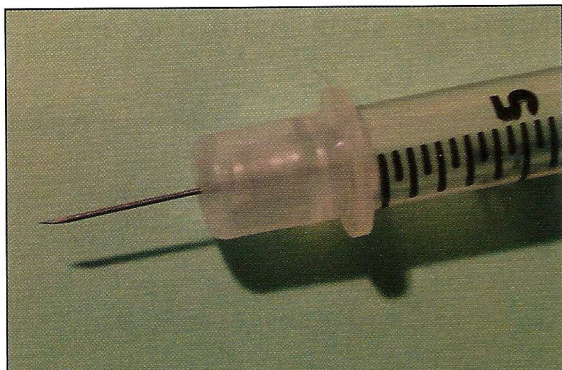


Figure 4 Botulinum toxin A was injected with a 0.3ml syringe and a 30G needle

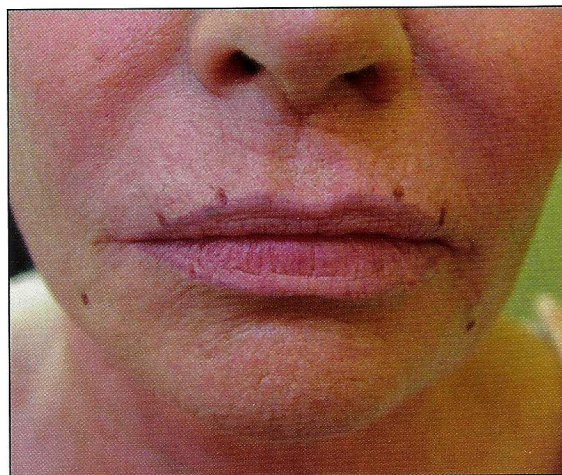


Figure 5 Patients are marked prior to treatment

▷ and three patients warfarin, for which there were no problems in either situation. Before and after photographs were taken.

Patients were evaluated at day 0, after 15 days, and then after 30 days. After this last session, patients were asked to quantify their satisfaction on a scale of 1-5 (1=no result; 5= best result), and the physician also quantified the result by patient examination, with particular attention to muscle power reduction, evaluating photographs, and quantifying any side-effects.

Personal technique

All patients signed an informed consent form before treatment (mandatory by law), where it is clearly stated that the botulinum toxin A treatment is an off-label indication. The only 'on-label' indication in Italy is the treatment of glabellar wrinkles^{3, 7, 8}. The treatment is performed in three sessions, the first two with botulinum toxin A, and the third with hyaluronic acid when needed. In the first session, botulinum toxin A is injected, while the second session evaluates the outcome and corrects if necessary.

Two different types of botulinum toxin were used (those allowed in Italy for aesthetic indications in glabella treatment):

- Vistabex 50U (Allergan) in 165 patients
- Azzalure 125U (Ibsen, Galderma) in only 15 patients, as it has only recently been introduced to the Italian market

- (Bocouture 50U (Merz Pharma), a third botulinum toxin A is now available on the Italian market, but was not used in this study).

In all cases, the author injected botulinum toxin A with a 0.3ml syringe with a pre-inserted 30G needle (Figure 4).

Session one

All 180 patients were treated with botulinum toxin A. As mentioned previously, 74 patients received botulinum toxin A alone, while 106 patients received botulinum toxin A and hyaluronic acid in combination. Analysis of perioral movement and infiltration of the toxin is always carried out in the first session. Patients are marked prior to treatment (Figure 5), and an anaesthetic cream (prilocaine and xilocaine as EMLA cream) is locally applied for at least 30 minutes. Injection points are decided in a standardised mode—four points in the superior lip and two points at the inferior.

One hundred and sixty-five patients were treated with Vistabex, always diluted with 1ml of saline solution so that one Vistabex unit is in 0.02ml. In these patients the author injected—in the first session and prudentially—0.5U Vistabex (0.01ml=one step of the syringe) for each point. In the 15 patients injected with Azzalure, the technique is rather different: the vial of 125U Azzalure was diluted with 0.25ml of saline solution with adrenalin 1:100 000. To make this solution the author diluted 0.1ml of adrenalin (1mg/1ml) in 10ml sodium chloride, and then 0.25ml of this solution is used to dilute the vial. In total, five Azzalure units are in 0.01ml (one step of the 0.3ml syringe).

The author injects only one Azzalure unit in each point. To be able to inject such a little amount, after the dilution described above, 0.01ml that contains exactly five Azzalure units is diluted up to 0.6ml with normal saline solution. This results in five Azzalure units in 0.6ml. Then 0.01ml (a little bit less than one unit of Azzalure) is injected in each point. The use of the 0.3ml syringe is mandatory to be able to clearly see all these little amounts. In no case did the author inject at any other point than the standard ones. The injections are always carried out at a superficial intradermal level, just on the vermilion border. Patients are advised that the results will begin to appear after 3-10 days, after which they will feel a slight reduction in movement. In approximately 30 days this feeling will completely disappear.

Session two

Fifteen days after the initial treatment patients undergo an evaluation to assess the effect of the first toxin infiltration. It is usually possible to see the reduction of the contraction ability of the orbicularis, which helps to correct the thinner wrinkles and reduce the deepest. A light extroflexion of the vermilion edge, owing to the ▷

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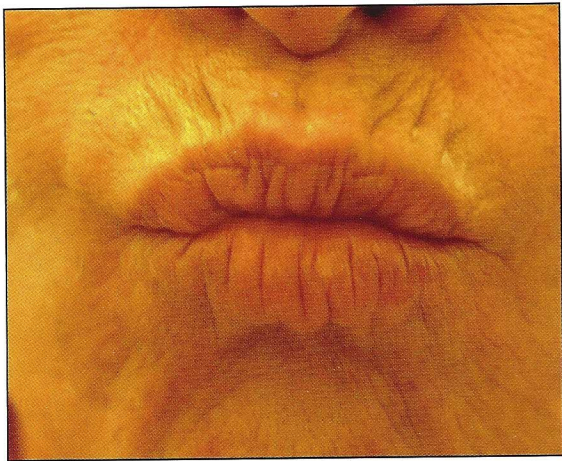


Figure 6 Before treatment with botulinum toxin A

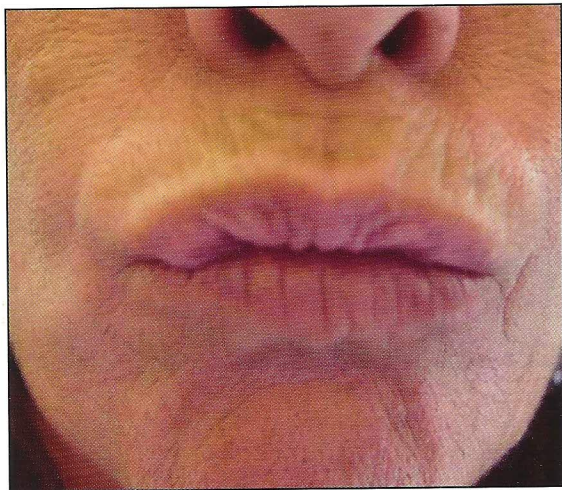
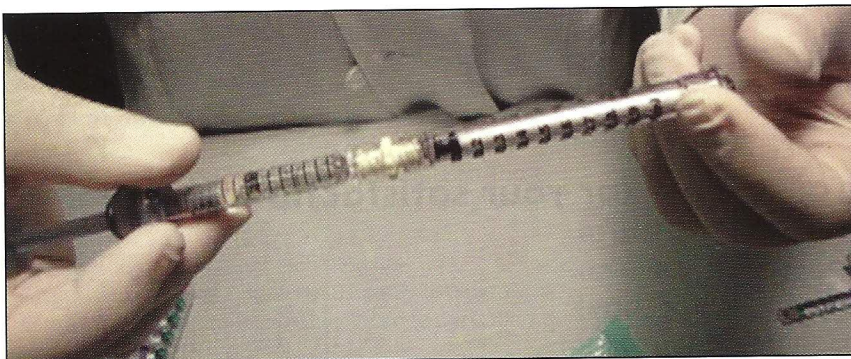


Figure 7 After treatment with botulinum toxin A

▷ relaxation of the superficial fibres of the orbicularis, is also visible, creating the pleasant effect of fuller lips. In *Figure 6* it is possible to see a patient before treatment, and in *Figure 7* the same patient 15 days post-treatment. Ten patients (6%) in the Vistabex cohort declared a scarce result and were retreated with a single dose of 0.5U for each lip, always intradermally. Three patients (1.8%) in the Vistabex group had an asymmetric response with aesthetic improvement only on one side of the lip—in this case the patient was asked to contract the muscle (the classic kissing movement), and it was possible to notice more movement of the lip that was

Figure 8 The syringes were joined with the two-way connector and, using a back-and-forth movement, the mixing is completed



less paralysed. In these cases, the next step was to administer a second toxin infiltration in the amount of 0.5U Vistabex in two points, according to the asymmetry determined in the less paralysed lip. The patients treated with Azzalure were never retreated. Most patients were re-evaluated 30 days after the initial infiltration.

Session three

In the second session, it is also decided whether to treat patients with hyaluronic acid or not: 15 days later, if retouched with botulinum toxin in this session, otherwise immediately. In this study, 106 patients (58.8%) were additionally treated with hyaluronic acid as lip fullness was still reduced.

All patients signed a further informed consent form for the injection of hyaluronic acid. The classic 'Paris lip' technique was performed in most cases, while only a minor volume improving technique was performed in only a few cases. The author did not use a truncal anaesthetic block as it tends to significantly change local conditions, altering the precision of the technique. Rather, the author prefers to use a local anaesthetic cream (EMLA) for 30 minutes before treatment. Also, the use of a 27G blunt cannula significantly reduces pain on injection. When possible, products with lidocaine were used⁴, but when the anaesthesia was not included in the vial, Carbocaine 3% was added (*Table 1*). In these instances, the following were used:

- The hyaluronic acid syringe provided by the company
- A sterile two-way connector
- A sterile 2ml syringe
- 0.2/0.3ml of Carbocaine 3% without adrenaline.

The syringes were joined with the two-way connector and, using a back-and-forth movement, the mixing is completed in a short time (*Figure 8*).

The author injected the edge of the lip using a 27G cannula, which makes the lip treatment possible in just a single injection (resulting in greater homogeneity and a much lower risk of haematoma). The technique is very simple: a little anaesthesia with 0.1ml Carbocaine 3% is injected near the lip commissure with a 25G needle (*Figure 9*), and the cannula is inserted (*Figure 10*) until the tip of the lip (*Figure 11*). No further anaesthesia is required. The same process is followed in the inferior lip (*Figure 12*). The central 'V', under the philtrum, and the philtrum columns were treated with a 27G needle at the end of the session as the anaesthesia provided was well induced. If

Table 1 Hyaluronic Acid used

| Product | Company | Patients treated (n=106) |
|----------------------|----------|--------------------------|
| X-HA ³ | Filorga | 38 (35.8%) |
| Juvederm ULTRA | Allergan | 20 (18.8%) |
| Juvederm ULTRA SMILE | Allergan | 5 (4.7%) |
| Regenyal Idea | Kaliderm | 16 (15%) |
| Restylane | Q-Med | 18 (16.8%) |
| Teosyal kiss | Teoxane | 9 (8.4%) |

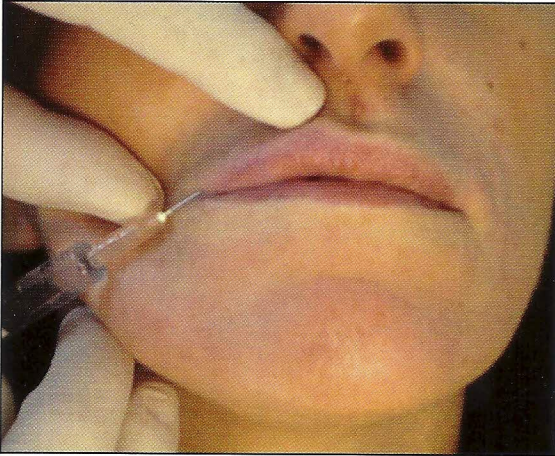


Figure 9 Anaesthesia is inserted near the lip commissure

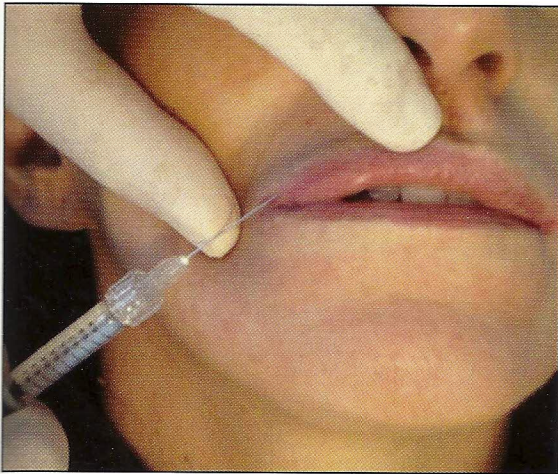


Figure 10 The cannula is inserted until the tip of the lip

necessary, vertical rhytides are treated directly using an intradermal implant.

Results

Botulinum toxin A

The toxin begins to take action after a period of 3-10 days, a little earlier than that in the upper third of the face. Aesthetic improvement was satisfactory and the patients were pleased with the results. The following parameters were documented:

- An obvious reduction of the wrinkles in the dynamic phase
- Light improvement in the static phase
- Increased projection of the lip edge.

Patients in the first cohort did not want further treatment with hyaluronic acid because they were already satisfied with the result of the toxin alone, and therefore avoided the discomfort of injecting the filler, which is much more traumatic than the toxin and with more visible consequences (e.g. oedema, haematoma, pain). All patients were satisfied and gave a result higher than 2 on the assessment scale, but most patients gave a result of 3-4 on the scale of 1-5, where 1 is a poor result and 5 is excellent. The average result was 3. The score of patients'

“ In all patients treated with botulinum toxin, there was a reduction in the amount of hyaluronic acid necessary for the correction. ”

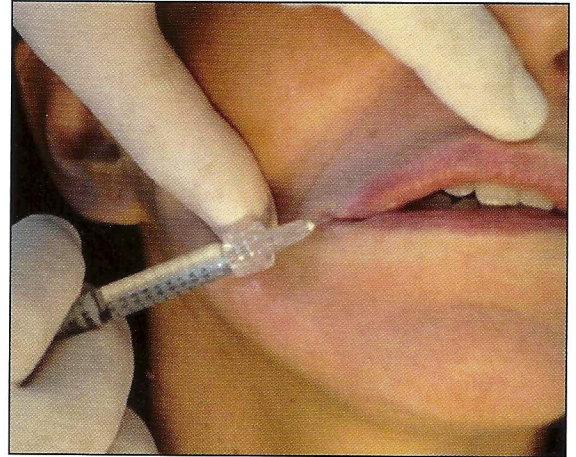


Figure 11 Hyaluronic acid is injected with a retrograde injection

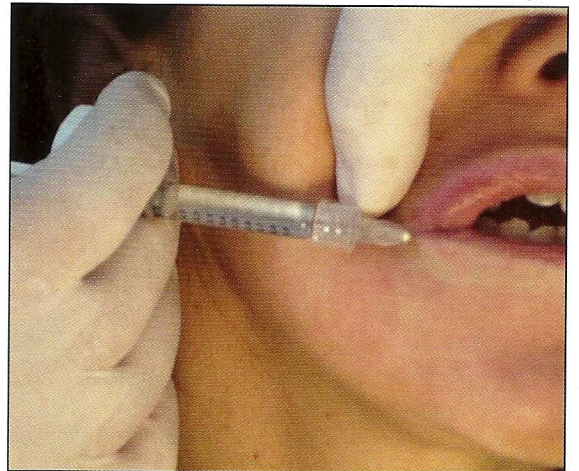


Figure 12 The same process is followed in the inferior lip

and physicians' satisfaction, and the final result after receiving botulinum toxin, are shown in *Figure 13* (overleaf). There is likely very little difference between Vistabex and Azzalure: Azzalure seems to be a little stronger than Vistabex, with the doses used in this case history, but further studies are needed to precisely evaluate the difference between the two products. They are not interchangeable.

Hyaluronic acid

Patients from the second cohort were injected using the Paris lip technique; only minor corrections were carried out in some cases, according to the author's philosophy. Results were always good, with most patients declaring a result of 3, using the same scale of 1 (poor result) to 5 (excellent result) (*Figure 14*—overleaf).

In all patients treated with botulinum toxin, there was a reduction in the amount of hyaluronic acid necessary for the correction.

Side-effects

The post-botulinum toxin feeling of patients is shown in *Figure 15* (overleaf). The patients were informed that the toxin begins to work after 3-6 days, after which, ▷

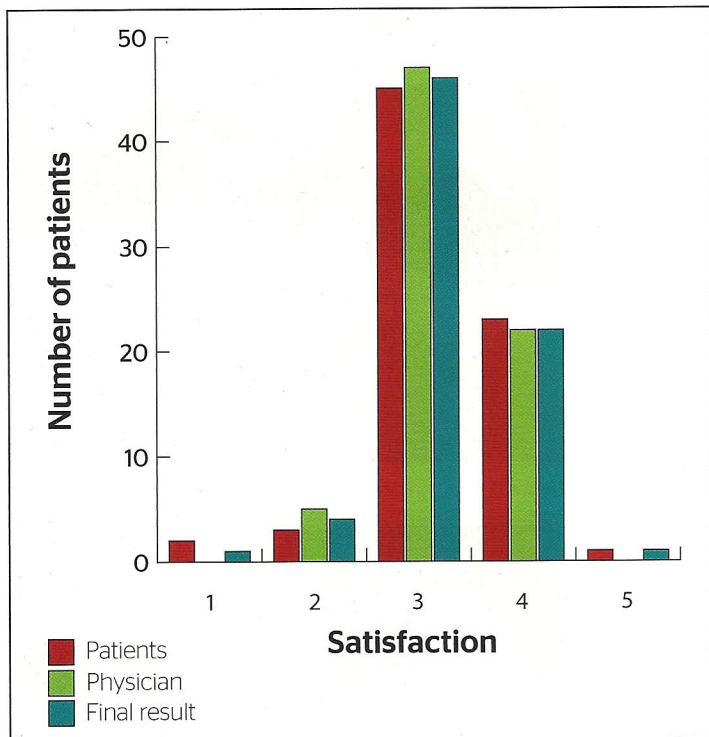


Figure 13 Patient, physician and overall satisfaction with treatment: cohort 1, botulinum toxin A only

▷ for a successive 2-15 days, 108 (60%) patients experienced:

- A loss of control over the perioral muscles (52.7%; 95 patients)
- A feeling of incontinence of the lips while drinking or eating, (46.1%; 83 patients)
- A feeling of a distorted mouth, or feeling that one is laughing in strange way or speaking differently (11.6%; 21 patients).

In reality, and aesthetically, nothing is visible, but the patient's perception will be altered. After no more than 15-20 days, the patient will naturally become accustomed to their perioral movements. None of these are 'real' side-effects, but merely the normal development of the toxin's effect, and patients must be advised in advance of any possible discomfort or unusual sensations. In 1.6% of the total patient population ($n=3$), a deviation of the midline of the upper lip was evident, demonstrating greater intake of the toxin in one side. In 6% of Vistabex patients ($n=10$), the results were too low and for this reason patients were reinjected. In 5.4% of Vistabex patients ($n=9$), the recommended doses (0.5U per point of botulinum toxin) were too high, with patients complaining of the same uneasiness even after 20 days; in 1% ($n=2$) even after 1 month. In the case of overdose, the only way to decrease the sensation of discomfort is by performing muscular exercises. All patients in the Azzalure population had the sensation of treatment and were not reinjected; 72 patients (40%) did not perceive any unusual sensation.

All the hyaluronic acid varieties used were proven safe; no case of significant side-effects occurred with this procedure. At the most, there was a little bruising and in a

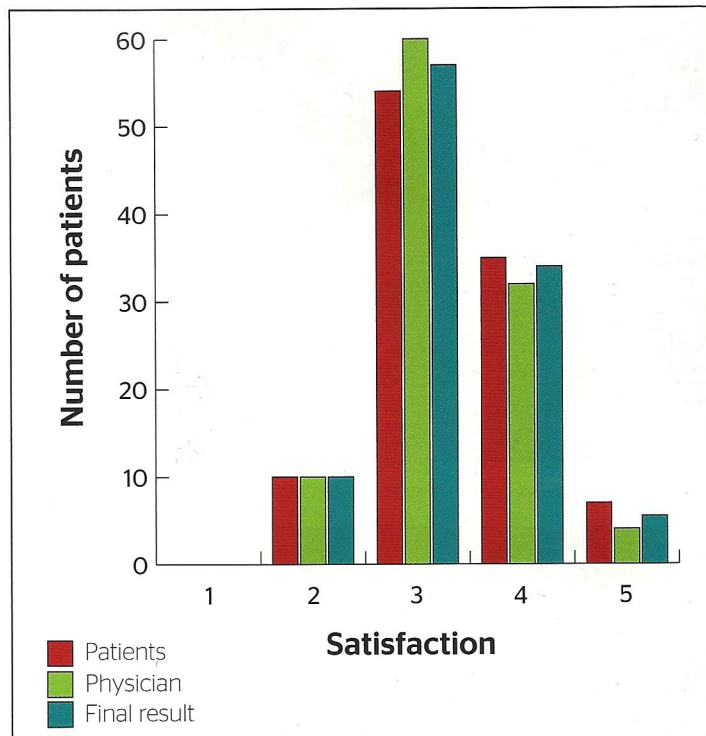


Figure 14 Patient, physician and overall satisfaction with treatment: cohort 2, botulinum toxin A plus hyaluronic acid

few cases, an oedema occurred. In no case were there any serious infections, but in one case herpes simplex occurred 10 days after the procedure.

Discussion

The fact that all the patients gave a positive result testifies to the safety of the procedure. Even if 60% of the patients complained of strange feelings, all reported sensations should be considered a normal effect of the toxin, and if patients are informed of this discomfort beforehand, there is no problem. The two patients who experienced ▷

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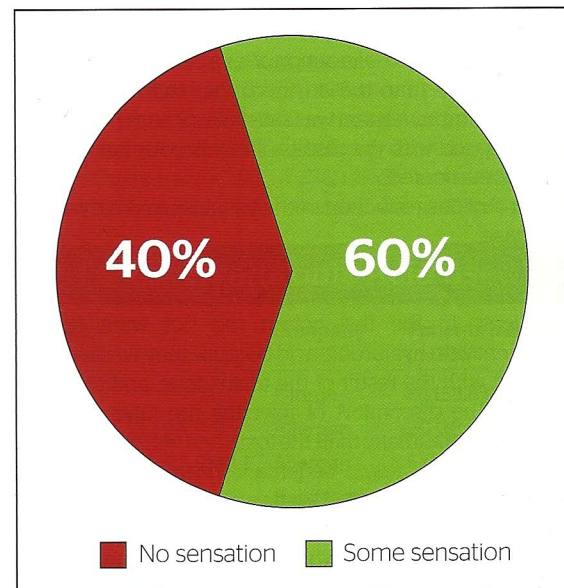
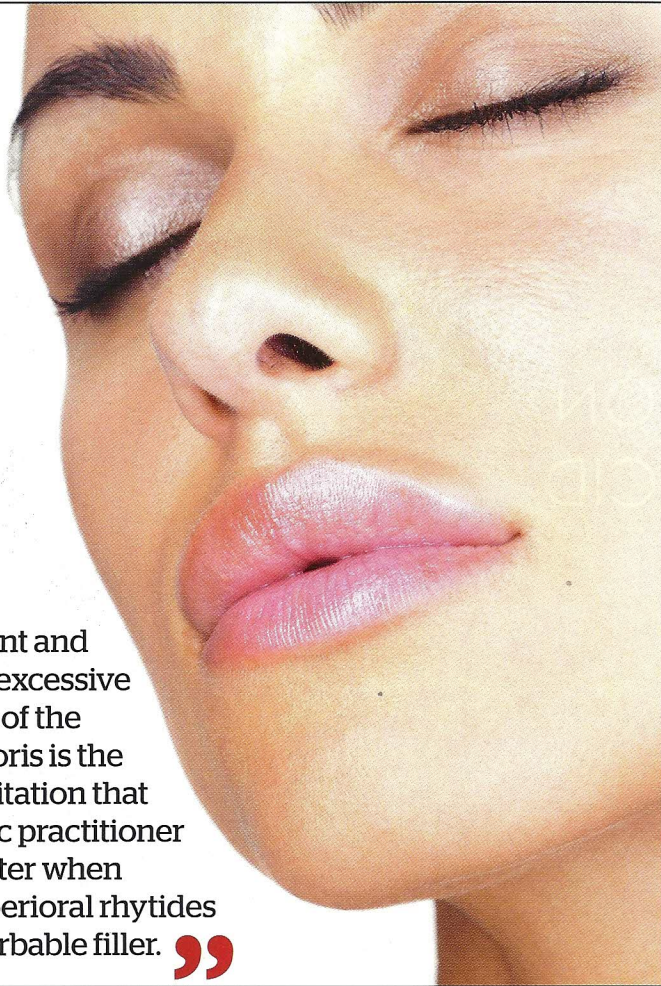


Figure 15 Post-treatment sensation and side-effects after botulinum toxin treatment

“Frequent and sometimes excessive contraction of the orbicularis oris is the greatest limitation that the aesthetic practitioner can encounter when correcting perioral rhytides using a resorbable filler.”



▷ discomfort for 1 month did not voice any complaints with regard to this prolonged effect, and ultimately perceived an excellent result of treatment. Lower, prudential doses used in our patients eliminated any eventual problem of ptosis of the lip, which did not occur in this study, and all other significant side-effects, occurred in other studies^{1,8-10}.

In most cases, using low doses (0.5U Vistabex or 1U Azzalure per point) was still effective. There were no patients who did not respond to treatment. The use of the 30U Becton Dickinson syringe is fundamental for the precision of the injected doses. It is interesting to note that many patients were satisfied with the toxin alone (highlighting, therefore, a new technique to be used as primary indication), and that the toxin infiltration reduces the frequency and the amount of filler injections. When used in conjunction with the toxin, the author never had to make any over-corrections—not even in those patients who complained of the durability of the filler when used alone.

This technique is particularly suitable for younger people, with increased movements, who have wrinkles mainly in the dynamic phase, and who are searching for a way to remove them. Currently, there are few techniques to treat these patients; surgery is premature,

heavy peelings and laser resurfacing is not easily tolerated, and fillers of whichever type improve but do not completely correct the problem of mimic wrinkles. In these patients, this technique can be considered an ideal solution, a 'gold standard'. What is important, however, is to make patients aware of all the strange feelings they will experience.

Conclusions

Frequent and sometimes excessive contraction of the orbicularis oris is the greatest limitation that the aesthetic practitioner can encounter when correcting perioral rhytides using a resorbable filler, which reduces both the duration and the quality of the result. It is clear that the use of botulinum toxin A can help, giving more relaxed tissues. Additionally, the thinner and superficial wrinkles, which are the most difficult to correct with fillers (hypercorrection is frequent), often disappear after using only the toxin. The wrinkles that, in the author's experience, demonstrate the best indication are those that appear only during the contraction of the orbicularis; this is the case in younger patients who are smokers. When used alone in these patients, the filler does not produce optimal results, and the duration time is unsatisfactory. The toxin has been proven to successfully obtain a good clinical result using lesser amounts of filler.

If well performed, side-effects are infrequent, always reversible, and of little concern for the patients, if well informed in advance. In the author's opinion, the greater side-effects described in previous reports are the result of elevated doses and incorrect injection sites. Often very low doses are enough to obtain good results. In some cases, finally, botulinum toxin can be used alone as a first-line treatment.

Declaration of interest Professor Redaelli is consultant, speaker and tutor for Filorga, Galderma, Allergan, Aventis and other medical companies. This article received no funding sources and is written purely from Professor Redaelli's experience.

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