

The Effect of the Treatment by Combining Hyaluronic Acid Filler and Botulinum Toxin A on the Upper Face

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ABSTRACT

Background and Aim: Recently, more people have better aesthetic satisfactions with the application of various treatment methods. Especially, development of botulinum toxins and facial fillers provide patients having folds with new hopes. We studied to clarify the aesthetic effect of the treatment by combining the injectable hyaluronic acid (HA) and botulinum toxin A (BTX-A). **Methods:** 115 patients complaining about folds in foreheads, glabellars, and lateral periorbital regions were selected. We made two groups; control group was treated only with injectable HA filler and experimental group was treated by combining HA and BTX-A. Both groups were followed for 8 months after injection. HA (Restylane) and BTX-A were together applied to the upper face folds including forehead, glabellar and crow's feet that were represented by mimetic muscles. We evaluated the correction and the maintenance effects in control and experimental groups at 0 and 8 months after treatments. All the experimental values were analyzed statistically with Student's *t* test of Microsoft Excel 2013. **Results:** All the patients in both groups had efficient fold corrections, but there was no significant difference of the rate of maintenance between 2 groups. **Conclusion:** On the upper face, combined treatments with the injectable HA and BTX-A were intended to have better early effects than with only a filler, and the combined procedure didn't have a significant difference in fold correction maintenance effects after 8 months.

Key words: Facial filler, Hyaluronic acid, Facial fold, Botulinum toxin, Aging.

INTRODUCTION

Recently, lots of fillers to correct facial aging signs are manufactured and widely used in aesthetic surgery.^[1,2] In 21st century, the hyaluronic acid (HA) fillers have been developed and widely used, and stabilized non-animal HA products made by the microbe cultivation are suggested as predominant fillers.^[3]

HA filler is an indispensable medical material in aesthetic surgery and the establishment of the treatment system with fillers is one of the necessary processes in enhancing the specialization level of medical service.

We have investigated to compare aesthetic effects of single HA filler treatment with combined treatment of HA filler and botulinum toxin A (BTX-A) at 8 months after injections.

MATERIALS AND METHODS

We recruited 115 patients (182 cases) among the facial aesthetic inpatients in General Dental Hospital of the Ministry of Public Health and Dental Hospital of Pyongyang from June 2017 to August 2019. Twenty-six men and 89 women who were 39 years old on average (range of 24-48 years) wanted to correct the facial folds. One hundred and fifteen consecutive patients were treated with facial intra-

dermal implant of hyaluronic acid gel (Restylane) on 182 regions in total.

Fine or superficial lines have not been treated. Filler injections were focused on minimizing the risk of bruise. Patients were recommended to avoid salicylate and anti-inflammatory drugs and doses of vitamin E greater than 400 IU daily, for seven to ten days before treatment.

Injection of Botulinum Toxin A

BTX-A was injected four-five days before or two weeks after HA injection. We used various injectable volumes on different regions; 30-40 units in forehead fold, 20-30 units in glabellar and 20-30 units in lateral periorbital region.

Injection of HA Filler

In linear threading, the filler was slowly injected during a needle withdrawal along the length of a facial region of desired enhancement. The treatment was done at once and the touch up had been allowed after 10-15 days. The average amount of material used for one patient was 1.3-1.4 ml. About 0.8ml in forehead, 0.4ml in glabellar, and 0.1-0.2ml in lateral periorbital region were used for optimal appearances. A local anesthetic solution (Xylocaine® Pump Spray

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10%, AstraZeneca, Sweden) was sprayed before the injection. Common antiseptic solutions had been used to disinfect the skin.

The filler had been inserted into the mid-dermis using 27 or 30 gauge needles, 13–20 mm long and beveled up, and injected to the fold with 30° angle to the plane of the skin longitudinally. Our technique consists of a line injection creating a continuous row of observable swelling without blanching and the insertion of the filler being done in withdrawing the needle. An immediate moulding with finger pressure on the inserted region could be done to correct possible uneven beadings of the product. A control group was treated with only HA filler, and an experimental group was treated with HA filler and BTX-A.

Statistical analysis of Data

Significant difference was done with Student’s *t* test of Microsoft Excel 2013. *P* value less than 0.05 was considered as statistically significant.

RESULTS

In the upper face, the combined treatment of HA filler and BTX-A was better in the facial fold obliteration effect than only with HA filler, but the maintenance effect of HA filler in the combined treatment had no difference with in the single use. The results were evaluated in all patients by subjective judgements of physicians and patients, and by photographic methods at 0, 1, 2, 4 and 8 months after injections.

The treatment effects aesthetic correction effect indexes were identical with the literature 3, but the evaluation percentage levels were a little different. They were “no improvement”, “slight improvement (1–50% correction)”, “moderate improvement (51–75% correction)”, “marked improvement (76–100% correction)” and “overcorrection”.

The rate of maintenance was estimated through the evaluation of the effect changes for 8 months after injections respectively. We determined

that the moderate and marked improvements were the treatment effective levels, and we counted the total numbers of the effective patients at 0 and 8 months after injection.

And we worked out the percentage of the all effective patients 8 months after injection over the effective patients at early stage.

DISCUSSION

The aging process is complex and single therapies have already proven to be inefficient in dealing with all the signs that appear with time. When analyzing the aging face, we can know that signs such as saggy skin, static and dynamic folds, folds appeared from various etiologies.

A clear understanding of the patients’ aesthetic goals is essential to achieving successful outcomes with cosmetic treatments. Management of patients’ treatment expectations is really important. Successful outcomes for all patients can be achieved by following a general plan that includes patient education and assessment. Patients know what they want, however it is the physician who understands the anatomical basis and aging process and who knows the compromise between the expectations of the patient and what is possible.

Patients’ goals and expectations must be consistent with realistic physician evaluations and recommendations. Physicians should discuss the details about the treatment such as the amount of filler necessary to achieve the desired correction, the costs of the filler, comfort techniques, potential complications, and the potential lasting time. Procedures achieving the successful correction effect with filler injection should be highly individualized in accordance with the patients. It is quite common for most patients to request the fold correction treatment with botulinum toxin A (BTX-A) only, because this product is widely advertised. In most cases, however injection of BTX-A into the several folds would result in

Table 1: Fold types.

Treatment group	Fold types			All
	Forehead	Glabellar	Lateral periorbit	
Control group	16	56	22	94
Experimental group	15	48	25	88
All	31	104	47	182

Table 3: Forehead fold injection effect.

Treatment group	Duration/Month		Rate of Maintenance (%)
	0	8	
Control group (n=19)	78.95	56.14	71.13
Experimental group (n=15)	86.64	62.20	71.79

Table 2: Response of the experimental group: forehead folds.

Estimation	Duration/Month														
	0			1			2			4			8		
	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph
No Improvement	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
slight improvement	0	0	0	0	0	0	0	0	0	3	3	3	6	6	5
Moderate Improvement	6	6	7	4	4	5	4	4	5	5	5	5	4	4	5
Marked Improvement	7	7	6	11	11	10	11	11	10	7	7	7	5	5	5
Overcorrection	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0

Es: Estimation; Pc: Physician; Pt: Patient; Ph: Photography

Table 4: Response of the experimental group: glabellar folds.

Es	Duration/Month														
	0			1			2			4			8		
	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph
No improvement	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Slight improvement	0	0	0	0	0	0	0	0	0	3	3	4	9	9	10
Moderate improvement	8	8	7	5	5	6	10	10	10	9	9	9	9	9	8
Marked improvement	40	40	41	43	43	42	38	38	38	36	36	35	30	30	30
Over correction	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Es: Estimation; Pc: Physician; Pt: Patient; Ph: Photography

Table 5: Glabellar fold injection effect.

Treatment group	Duration/Month		Rate of Maintenance (%)
	0	8	
Control group (n=56)	98.21	77.38	78.81
Experimental group (n=48)	100.00	80.56	80.56

an unhappy patient because this would have a little effect on the different depths of the folds.

Instead of using single method exclusively, nowadays the treatment method by combination of several materials is the trend in aesthetic surgery. Therefore the physicians should discuss with the patients that multiple therapies should be applied, although unfortunately this might not be obvious to patients. Patients should be educated to understand that the most natural appearance that can be obtained involves the use of multiple treatments.

The physician should point out what must be treated; whether a surgical or nonsurgical procedure should be performed. In general, saggy skin is treated with surgery, dynamic folds with BTX-A, and folds with fillers. Patients start to realize what can be treated with these three types of procedures, and even when everything is needed to promote a real improvement.

The forehead and glabellar regions are characterized by extensive mimic movements of three main muscles; occipitofrontal, corrugator, and procerus. Horizontal forehead lines are caused by the action of the occipitofrontal muscle. The vertical glabellar folds are the products of the continuous contractions of both corrugator muscles. The horizontal lines in the glabellar region are due to pronounced procerus muscle activity. "Crow's feet" are folds extending laterally from the periorbital region and are usually the sign of aging.

BTX-A is the first-line treatment for folds of the glabella; biodegradable injectable fillers should come as a second step in this region. Do not treat with fillers that might be better treated with another method. Lasting time of the biodegradable fillers has a limitation on certain regions that are affected by the muscles directly. Inhibition of muscular activity with BTX-A has been the solution to this problem in various regions, especially in the upper third of the face. Any remaining superficial lines above the eyebrow after treatment of the upper third with BTX-A can

easily be corrected with a fine biodegradable filler. Horizontal lines in the forehead are due to excessive movement of the frontalis. BTX-A is usually the single method needed in this region. But depending on the skin thickness and dermal injury, however, fillers may also be needed. After the effects of BTX-A are completed, fillers can be injected into the remaining folds.

Before injecting a filler for forehead and glabellar folds it is recommendable to pretreat this region with BTX-A. The combination of BTX-A and an injectable filler usually leads to a better overall result. BTX-A should be injected 2 weeks before the filler, although both procedures can be performed at the same time for this region.

Glabellar lines result from the action of the corrugator and procerus muscles, and the muscle group involved in the production of crow's feet in the lateral periorbital region is the orbicularis oculi that rings the orbit. BTX-A is the optimal solution to treat this region, and fillers may be needed as complementary treatment. The facial aesthetic treatment needs compositive and overall procedures, and therefore all non-harmonious sites of the face cannot be completely corrected with only one treatment method.^[4-6] Recently, some reports told us that with help of the clinical filler introduction, the combined treatment with HA filler and BTX-A enhanced the fold correction effects.^[7] The clinical efficacy examination of HA filler was conducted in accordance with the ministry of public health and the academy of medical science, and as a part of that, the evaluation of the combined treatment effect of HA filler and BTX-A in the upper face was performed.

In the upper face, patients had folds in several regions; forehead, 31 cases (17.03%), glabellar, 104 cases (57.14%), and lateral periorbital region, 47 cases (25.83%). And the combined treatment of HA filler and BTX-A were 88 cases. Using combined treatment, the early forehead fold correction effect (average 86.64%) was marked improvement and the effect after 8 months (average 62.20%) was moderate improvement, and 8 months post-injection effect was 71.79% of the early injection effect. Comparing the effects of single and combined treatments, the early filler effect in the combined treatment was remarkably higher than the single use (56.14%). It means that the combined treatment has the better aesthetic result than the single use of HA, especially in the early stage. Analyzing the 8 months maintenance effect in the aesthetic aspect, the use of single HA filler was 71.13% and the combination was 71.76%, so there was no significant difference.

We can know that combined treatment in the forehead fold can get the better aesthetic effect than the single use, but can be 71.76%, so the

Table 6: Response of the experimental group: Crow's feet.

Es	Duration/Month														
	0			1			2			4			8		
	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph	Pc	Pt	Ph
No Improvement	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
slight improvement	8	8	7	5	5	6	5	5	6	6	6	6	12	12	10
Moderate Improvement	7	8	7	8	8	7	8	8	7	10	10	9	8	9	9
Marked Improvement	10	9	11	12	12	12	12	12	12	9	9	10	5	4	6
Over Correction	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Es: Estimation; Pc: Physician; Pt: Patient; Ph: Photography

Table 7: Crow's feet injection effect.

Treatment group	Duration/Month		Rate of Maintenance (%)
	0	8	
Control group (n=22)	65.15	57.57	88.34
Experimental group (n=25)	69.33	54.67	78.88

Table 8: Rate of maintenance.

Treatment group	Duration/Month		Rate of Maintenance (%)
	0	8	
Control group (n=94)	80.77	64.09	79.34
Experimental group (n=88)	85.32	65.81	77.13

duration of maintenance. In glabellar folds, the combined treatment effects in the early stage (100%) and 8 months post-injection effect (80.56%) were all marked improvement level satisfactorily. Particularly the single HA filler effect in the glabellar fold was on a very high level in the early stage after injection, and also had kept the high level for 8 months equal with the combined treatment effect. Comparing the effects of both treatment methods, combined treatment effects in the early stage and 8 months post-injection were better than the HA single use effects (98.21%, 77.38%).

The glabellar fold shows that it is the effective treatment region for both BTX-A and HA filler. The maintenance effects for 8 months were respectively 80.56% and 78.81% in combined and single use, and they were not different significantly. In the lateral periorbital region, the 8 months post-injection maintenance effect of the combined treatment was 78.88%. The both effects for the early (average 69.33%) and 8 months (average 54.67%) were all moderate improvement levels. The 8 months post-injection treatment effects of the combination and single use were all slight improvement levels (54-57%). In the maintenance effects of combination and single use (78.88%, 88.34%), the combined effect was not proved better than the single use of HA filler. Fold correction and maintenance effects of both treatments has no significant difference,

so we can know that the lateral periorbital folds were not effective for HA filler.

In the combined treatment, we didn't find out the difference, and also the effects for early and 8 months were better in glabellar and forehead except for the lateral periorbital folds. Generally, the 8 months rates of maintenance of single HA and combined treatments were 79.34% and 77.13%, and they had no significant difference. Efficacy duration of BTX-A is about 3 months and the absorption half-life of the injectable HA is about 14 months.^[4] And the both medical drugs have different action mechanisms in the tissue so the effects don't combine pharmacologically. They control the fold formation respectively and they provide their fold correction effects.

CONCLUSION

We can conclude that in clinical practice HA filler and combined treatment with BTX-A can be effectively used to correct the folds but the durations of maintenance of two groups were not satisfactorily maintained. There was no evidence of major general side effects.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

HA: Hyaluronic Acid; **BTX-A:** Botulinum Toxin A.

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