
A PROSPECTIVE STUDY OF EVALUATION OF THE RESULTS ACHIEVED WITH THE APPLICATION OF A NEW GEL OF HYALURONIC ACID NON ANIMAL ORIGIN (PERFECTHA DERM SUB SKIN) FOR MALAR AND MENTAL ENHANCEMENT

AUTHORS

Daniel Vasconcellos Regazzini¹, MD. Jamel Fares², MD.

ABSTRACT

INTRODUCTION

Many signs of aging are due to the loss of subcutaneous fat. Dermal fillers are non-surgical cosmetic treatments used to restore facial volume. Perfectha Derm Sub Skin is new hyaluronic acid sub-dermal facial filler.

OBJECTIVE

The objective of this study was to assess its effectiveness in maintaining increased volume for up to 18 months post-treatment and its safety.

METHODS

Prospective record analysis was made for 126 patients (116 females, ten males; mean age: 50 years) who received Perfectha Derm Sub Skin injected into subcutaneous and/or supraperiosteal plane. All patients were assessed at baseline and at 2, 4, 8, month and 12-18 months post-injection.

RESULTS

Patients all showed a persistence of benefit during the post treatment observation period of up to 72 weeks. Six patients had minor side effects that resolved with local treatment and time. Seven patients had second injections to complete augmentation without complications.

CONCLUSIONS

Perfectha Derm Sub Skin provides aesthetic improvements according to investigator and patient assessment for up to 18 months post-treatment. Perfectha Derm Sub Skin is a useful injectable agent to augment and lift upper cheeks and re contour chins.

INTRODUCTION

For people requiring large volumes to shape facial contours, add volume to a sunken mid face, or correct asymmetry, the options today are limited. Fat injections for adding volume, solid implants for cheeks and chin enhancement, face lift and injectable permanent or semi-permanent products are some of the alternatives used.

There are numerous soft-tissue fillers, and they can be divided into three main categories: temporary biodegradable, semi-permanent biodegradable and permanent non-biodegradable filler materials.

1. Daniel Vasconcellos Regazzini: Plastic Surgeon and Entitled Member of the Brazilian Society of Plastic Surgery and member of the international Society of Aesthetic Plastic Surgery.

2. Jamel Fares: Plastic Surgeon and Entitled Member of the Brazilian Society of Plastic Surgery, Member of the Brazilian Medical Association, Member of the Paulista Association of Medicine, Member of the Institute of Plastic Surgery of Santa Cruz and Active Physician of the Plastic Surgery Service of the Avicenna Hospital in Sao Paulo.

Nonpermanent fillers also known as temporary biodegradable or reabsorbable fillers include polylactic acid, collagen, and calcium hydroxyapatite. Injectable silicone, polymethylmethacrylate microspheres and polyacrylamide gel are permanent fillers. Injected autologous fat can be nonpermanent or permanent. Injectable hyaluronic acid derivatives are the most commonly used reabsorbable dermal fillers for soft-tissue augmentation today, and have replaced collagen as the standard injection material.

Leading experts are also beginning to classify fillers via their mechanism of action; Volumizers, volume fillers, and Stimulators, tissue stimulating agents. Volumizers increase volume and fill out skin directly. Stimulators can also directly create volume, but primarily cause a foreign body reaction over a limited time, stimulating a long-term or permanent collagen deposition. Some filler exhibit both actions and fall into both categories.

With the trend towards less invasive and nonpermanent alternatives to plastic surgery, the use of injectable filler materials for facial rejuvenation and correction of soft-tissue defects is becoming increasingly popular. These materials provide volume expansion within the dermis, thereby smoothing out overlying facial wrinkles and enhancing facial contours. Ease of application, minimal procedural discomfort, and rapid patient recovery make injectable fillers well suited for outpatient use. Ideally, a filler material should be biocompatible, nontoxic, nonimmunogenic, and nonmigratory.

Several biomaterials have been developed, such as bovine collagen, autologous and allogeneic human collagen, autologous fat, fibroblasts, and hyaluronic acid. However, although they are largely biocompatible, reabsorption and lack of sustained cosmetic effect are major drawbacks. Hyaluronic acid products have been demonstrated to have a good safety profile, and few complications have been reported. The hyaluronic acid product Perfectha Derm Sub Skin is produced from a hyaluronic acid preparation obtained by bacterial fermentation. The use of a non animal origin source is thought to reduce the likelihood of antigenic contamination and subsequent hypersensitivity reactions.

The Non animal origin hyaluronic Acid offers a longer-lasting aesthetic effect than bovine collagen or avian hyaluronic acid in facial soft-tissue augmentation, and a potentially lower risk of inflammatory reactions. Perfectha Derm Sub Skin is a new non animal origin Hyaluronic Acid product indicated for deep subcutaneous or supraperiosteal injection to replace volume loss in facial adipose tissues and create more defined facial contours.

The main aim of this study was to evaluate the efficacy, safety and durability of Perfectha Derm Sub Skin product in the correction of depletion in cheekbones and chin.

OBJECTIVE

The main objective of this study was to evaluate the aesthetic result, the effectiveness, safety and duration of treatment with Perfectha Derm Sub Skin, in the treatment of depletion of cheekbone and Chin.

A group of treated patients has been studied for more than 1 year (18 months), Perfectha Derm Sub Skin was injected to the subcutaneous plane of the upper cheeks and supraperiosteal plane of the chin to observe efficacy of augmentation and side effect profile, and further observations were made of the duration of benefit.

METHODS AND PATIENTS

Patients treated were those who requested augmentation of upper cheeks or who desired a change of chin contour. An inquiry was made on general medical conditions and ease of bruising. Medications such as aspirin and non steroidal anti-inflammatory agents were discontinued at least 7 days before the procedure.

From October 2006 to April 2008 a total of one hundred and twenty six (126) adult patients received subcutaneous and/or supraperiosteal injections of Perfectha Derm Sub Skin. Treatment was carried out at two sites (Brazil and Colombia) Brazil treated 66 patients (60 females and 6 males) and Colombia treated 60 patients (56 females and 4 males) with a mean age of 50 years. (Table 1)

Inclusion and Exclusion criteria as follows:

Inclusion Criteria:

Subjects eligible for inclusion were between the ages of 30 and 55 years, were capable of providing informed consent, and had moderate to severe mid-face volume loss as judged by the physician evaluators. Subjects also could not receive any other facial procedures through the 18-month follow-up, and had to agree and be able to attend all scheduled follow-up visits. Patients were counseled as to the benefits and risks of the experimental treatment, and were accepted for treatment only after providing informed consent.

Exclusion Criteria:

- Previous treatment with hyaluronic acid, collagen and other fillers within 1 year prior to the study
- Known hypersensitivity to hyaluronic acid products
- Cancerous or pre-cancerous lesions on the mid-face
- Presence of pre-existing illness or injury that may increase study risks
- Active or chronic skin disease, inflammation or related conditions, such as infection, psoriasis and herpes zoster in mid-face.
- Patients that have undergone procedures based on active dermal response (e.g. laser and chemical peeling procedures), within 6 months prior to study entry.
- Any condition which in the opinion of the investigator made the patient unsuitable for inclusion (e.g., patients not likely to avoid other treatments, patients not likely to stay in the study for eighteen months, or patients that missed two consecutive follow up visits including the final one).

TABLE 1. Details of Patients Treated with Perfectha Derm Sub Skin to the Malar and Mental Facial Zones

Gender	Mean Age (Years)	Sites Injected*	Volume Injected (Mean)	Post treatment Observation Times
116 female 10 male	50	Malar Mental	109 3 mL (each side) 17 4 mL	2-72 weeks

*Four patients had both malar and mental zones injected.

The treatment was given in one or two sessions only. At baseline, the patients received an injection of approximately 1.5-2.0 mL hyaluronic acid in each cheek and 2mL of each side of the mental area.

The volume of Perfectha Derm Sub Skin injected was left to the discretion of the treating physician and noted. Average volumes were calculated.

All the injections were performed by the same plastic surgeon at the out-patient clinic of the Department of Plastic Surgery of each country hospital. The skin area was pen-marked with the patient in an upright position before the patient lay down for treatment. Under local anesthesia and previous asepsis and antisepsis a sharp 18-gauge cannula was used to perforate the skin laterally, just below the cheek bone. A blunt-tipped cannula with side-exit (1.2 x 70 mm; 18 gauge) was then inserted downwards and subcutaneously on each side, to make a tunnel. The tunnel was then filled with Perfectha Derm Sub Skin gel while the cannula was being retracted. Filling with Perfectha Derm Sub Skin was carried out using a fanning injection technique. At the end of each treatment, the cheeks were gently massaged in order to shape the filler material to achieve optimal contour.

For the chin treatment of Perfectha Derm Sub Skin gel the technique was direct under the muscle, no fanning technique applied. Following this, the entry areas were cleaned and local pressure was applied for hemostasis.

Effectiveness

The clinical effectiveness assessments were performed at:

- The treatment visit (pre-treatment assessment)
- When an optimal cosmetic result was obtained (baseline)
- At the follow-up visits: 2, 4, 8,12, and 18 months post baseline

Patients were evaluated using digital photography and clinical examinations, which included the use of a scale to measure satisfaction with facial appearance. Following each treatment and at each respective follow up, patients were asked to complete a questionnaire about the following adverse events: swelling, tenderness, pain, redness, lumps, hematomas and fever. Patients were assessed using the Global Aesthetic Improvement Scale.

Clinical Evaluation

Global Aesthetic Improvement Scale (GAIS)

The Global Aesthetic Improvement Scale is a five-grade subjective test for efficacy analysis. The physician and patient independently

compared the preoperative photograph with the treated face and answered the question: ‘How would you describe the degree of improvement?’ Possible responses were (1) very much improved, (2) moderately improved, (3) somewhat improved, (4) no change or (5) worse. (Table 2).

Table 2. Global Aesthetic Improvement Scale (GAIS).

Rating	Description
Very much improved	Optimal cosmetic result for the implant in this patient.
Much improved	Marked improvement in appearance from initial condition, but not completely optimal for this patient. A touch up will slightly improve the result.
Improved	Obvious improvement in appearance from the initial condition, but a touch-up or re-treatment is indicated.
No change	The appearance is essentially the same as the original condition.
Worse	The appearance is worse than the original condition.

RESULTS

One hundred and twenty six patients (126) were initially enrolled in the study; however, 7 were lost to follow-up and were not included in the data analysis. In all 7 cases, the subject expressed an inability to meet commitments for follow-up visits. There was no evidence that treatment considerations (eg, adverse effects or lack of efficacy) were involved.

Patients all showed a persistence of benefit during the post treatment observation period of up to 72 weeks. Six patients had minor side effects that resolved with local treatment and time. Seven patients had second injections to complete augmentation without complications.

The patients and injectors observed augmentation of the areas injected. On subsequent clinic visits, patients were asked whether they felt they had sufficient or insufficient augmentation. Seven patients decided to have further augmentation, where between 1 and 2 mL of further material was injected in the same location as the first implant. All injected patients were satisfied with the procedure. Injectors graded the results as very much improved, much improved or improved in most cases.

Efficacy Results

Two-month

At 2-month follow-up, 116 of 119 (97%) patients were rated as very much improved, much improved or improved by the physician evaluator regarding malar and chin augmentation and three patients were rated as no change. One hundred and seventeen of 119 (98%) patients rated themselves as improved, much improved, or very much improved using the GAIS scale and only two patients rated themselves as no change (Table 3). At the 2-month visit, touch-up injections were recommended for 5 patients in the malar area and 2 patients in the mental area with an average volume of 1mL per side. No more touch ups were administered after this period.

Four-month

Only 118 patients were available for evaluation at the 4-month follow-up visit. One patient missed her 4-month follow-up visit, but returned for the rest of the follow-up visits (8, 10, 12 and 18 months). Of the 118 patients evaluated, the physician evaluator rated 118 (100%) as very much improved or improved. Equally 118 (100%) patients rated themselves as very much improved or improved. (Table 4)

Eight-month and Twelve month

All 119 patients were available for the eight month and twelve month follow up visit and the physician evaluator rated 119 (100%) between the parameters of very much improved, much improved and improved (Table 3). Independently the 119 (100%) patients rated themselves on the GAIS scale also as very much improved, much improved or improved (Table 4).

Eighteen-month

Final evaluations were performed at 18 months. Ratings remained high, with aesthetic ratings by the physician evaluator of very much improved or improved for 119 of 119 patients (100%). Similarly, all 119 patients (100%) rated themselves as very much improved, much improved, or improved. (Table 4).

At the 18-month visit, patients were also asked the following questions regarding their experience with Perfectha Derm Sub Skin for malar and mental augmentation: (1) ‘‘Were you pleased with the final outcome?’’; and (2) ‘‘Would you recommend this procedure to a friend?’’. Of the 119 patients who completed the study, 118 (99%) identified themselves as pleased with the final outcome, and 116 (97%) said they would recommend the procedure to a friend. Seven patients opted to receive touch-up treatments at 2 months.

Table 3. Two-Month - 18 Month Efficacy Results (n=119)

	Physician Evaluator Aesthetic Rating									
	Very Much Improved		Much Improved		Improved		No Change		Worse	
	N	%	N	%	N	%	N	%	N	%
2-Month	48	40	64	54	4	3	3	3	0	0
*4-Month	57	48	54	46	7	6	0	0	0	0
8-Month	62	52	55	46	2	2	0	0	0	0
12-Month	66	55	50	42	3	3	0	0	0	0
18-Month	54	45	60	50	5	4	0	0	0	0

* For the 4-Month follow up visit n=118

Table 4. Two-Month-18 Month Efficacy Results (n=119)

	Patient *GAIS									
	Very Much Improved		Much Improved		Improved		No Change		Worse	
	N	%	N	%	N	%	N	%	N	%
2 Month	52	44	60	50	5	4	2	2	0	0
**4 Month	60	51	56	47	2	2	0	0	0	0
8 Month	60	50	59	50	0	0	0	0	0	0
12 Month	68	57	49	41	2	2	0	0	0	0
18 Month	52	44	60	50	7	6	0	0	0	0

*GAIS= Global Aesthetic Improvement Scale

** For the 4-Month follow up visit n=118

DURATION

Duration of improvement remained for the time of observation of this preliminary treatment study, i.e., up to 72 weeks. The authors anticipate continued persistence for varied times among the treated patients and see no reason to not re-treat.

SIDE EFFECTS

Local adverse reactions are consistent with those expected of an alloplastic filler material and appear to be related to the injection procedure/site rather than to the product itself. Adverse events were reported in only 6 of 119 patients (7%). Two patients reported mild edema and hematoma, which resolved in less than 2 weeks. Four reported mild ecchymosis and edema following initial treatment and mild edema after receiving touch-up treatment. The effects resolved within 5 days.

DISCUSSION

Patients who are seeking facial rejuvenation may not explicitly request cheek or cheek augmentation. Nonetheless, restoring lost volume in the cheeks or chin can have a rejuvenating effect on the face as a whole. This study examined whether a semi permanent, volumizing filler, such as Perfectha Derm Sub Skin gel, which is generally placed deeper and is also more long-lasting than current temporary fillers, could provide a viable option for patients with mid-face volume loss who do not yet require or desire surgical rejuvenation.

In this pilot study, malar and mental augmentation with injectable Hyaluronic Acid (Perfectha Derm Sub Skin) proved to be effective, easy to administer, and safe. Adverse events that did occur were minor in both nature and degree (eg, bruising and edema), were limited to the injection site, and resolved spontaneously within several days; such effects are consistent with the use of fillers for soft tissue augmentation in general. Importantly, there were no cases of granuloma formation, development of nodules or product migration. Patient comfort was enhanced with the use of anesthesia.

A “tracking” technique was used to deposit multiple threads of material in a cross-hatching fashion. Given the relatively large surface area involved in malar augmentation, cross-hatching and layering of material in many tissue planes at or below the subdermis to provide a robust correction is recommended. For most patients, an injection of 1.5 – 2mL material per side (average: 3mL) was sufficient to produce significant improvement. At the 2-month visit, 7 patients received touch-up treatments. The request for touch-ups at 2 months was generally based on whether patients desired additional correction and whether the physician felt that additional correction could realistically be achieved. Perhaps the best measure of patient satisfaction is that 118 (99%) of 119 patients indicated that they were pleased with the final outcome. Equally important, all but 2 of those patients said they would recommend malar or mental augmentation with Perfectha Derm Sub Skin.

CONCLUSIONS

Our results show that hyaluronic acid can produce significant improvements in the restoration of facial fat thickness. It was effective in achieving aesthetic correction of the cheek, and chin. The product provided durable improvement for most patients for at least 1 year. There were no serious adverse effects and no treatment interruptions because of side effects. A non animal origin hyaluronic acid product with larger particles appears to be a useful supplement to fillers for patients in need of treatment for facial definition. Perfectha Derm Sub Skin is a useful injectable agent to augment and lift upper cheeks and recontour chin.

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