Facial Corrections for Lipoatrophy in HIV-infected Patients: Treatment with Polyacrilamide Hydrogel injections

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Summary

This open-label study takes aim at the valutation of the efficacy and safety of facial injections of an Polyacrilamide Hydrogel (PAIG), in HIV-positive people that showed different level (severe, moderate and mild) of facial lipoatrophy.

This is a typical AIDS-related pathology that involve a loss of subcutaneous fat in the face, especially in cheeks, temples and nasolabial folds, and other parts of the body, and often it consequently cause some mental rebound (lack of self-interest or loose of self-esteem).

36 HIV-positive subjects with facial lipoatrophy were enrolled.

Every treatment consisted of the injection of 1 to 2 vials of PAIG on the first day, and every 4 weeks for some months, according to the level of facial lipoatrophy. We previously advised each one of the subjects to avoid sunburn in the injection’s area.

Patient’s valuation has been done by facial ecozonography, along with clinical examination.

Withal we took standard photographs before and after the treatment, scheduled for successive 12th, 24th and 48th week.

100 percent of our patients have been pleased with the aesthetic result, and they all judged excellent elasticity and consistency in the treated area after twelve months.

Pain (scale 0-10) related at moment of the injection was reported in all patients.

Excellent results has been obtained in the parietal area and lower third of the face, and also in the upper and lower jaw.

The advantage of this hydrogel relates to its non-biodegradability and its important tolerability. Our product does not generally cause allergic reaction or other immunological effect either in animals or in humans; above all it does not migrate.
Riassunto

Questo studio sperimentale ha lo scopo di valutare l’efficacia e la sicurezza dell’uso di un Polyacrilamide Hydrogel (PAIG) per iniezioni nel volto, in pazienti HIV-positivi che presentavano vari gradi di lipoatrofia faciale (severa, moderata e lieve).

Questa alterazione cutanea è una tipica conseguenza dell’infezione da HIV che comporta la perdita dello strato di grasso sottocutaneo del volto (in particolar modo a livello delle guance, delle tempie e dei solchi naso-labiali) e di altre sedi corporee; essa quindi provoca frequentemente ripercussioni a livello psichico quali perdita di autostima e di interesse di sé.


La valutazione dei pazienti è stata condotta tramite ecofonografia faciale e periodico esame obiettivo. Abbiamo inoltre documentato con fotografie standard le condizioni pre e post trattamento, programmate a 12, 24 e 48 settimane.

Tutti i nostri pazienti sono rimasti soddisfatti del risultato estetico. Tutti hanno giudicato eccellente l’elasticità e la consistenza cutanea nell’area trattata a 12 mesi di distanza.

Per ogni paziente abbiamo riportato su scala (range 0-10) l’intensità del dolore al momento dell’iniezione.

Sono stati ottenuti risultati eccellenti nella zona temporale come nel terzo inferiore del volto, sia a livello della mascella che della mandibola.

Gli importanti vantaggi che offre questo hydrogel sono la sua tollerabilità, il non essere biodegradabile, e soprattutto il permanere nel sito di iniezione senza spostamenti. Il prodotto generalmente non provoca reazioni allergiche o altri effetti immunologici né negli uomini né negli animali.
INTRODUCTION

Body fat changes in HIV positive patients are known as lipodystrophy. Three patterns of body fat changes are being seen in people with HIV who are taking combinations of anti-HIV drugs (retro transcriptase or protease inhibitors), called Highly Active antiretroviral Therapy (HAART). One pattern involves gaining of fat, on the abdomen/belly (central fat), between the shoulders or around the neck or in the breast (mostly in women). The lipoatrophy consists of losing of fat, and the third pattern is a mixture of gain and fat loss. The majority of people develop these changes experience a mixture of both types of body fat changes (in fact, is used sometime the term ‘fat redistribution’) (1).

Lipoatrophy is characterized by a loss of subcutaneous fat in face, in the arms, legs and buttocks. Only this particular kind of fat loss is specific to HIV infection: indeed, fat gain may be caused by metabolic changes that also occur in HIV-negative people. This pathology proceeds by grading scale, mild, moderate and severe, and it is also connected with genetic predisposition. There is recent evidence of a role for ApoC3-455 (4). Studies have shown that after three years on a combination of nucleoside analogues and a protease inhibitor, 30 to 40% of people will develop body fat changes (1).

The arms and legs show prominent veins, buttocks becomes shrunken. The facial results is a wasting: the loss of sub-cutaneous fat take place especially in the cheeks (called ‘bolla adiposa of Bichat’), in temple’s area and around oral region (1). Consequently, this feature’s alteration may cause many mental rebound, most of all severe psychological disturbances such as depression, anxiety, social isolation, reduced confidence and self-worth, lack of self-interest, and in the end, loss of self-esteem (1, 4, 5).

Different strategies have been developed to reduce the visible effects of these alterations. Studies are underway to see if any medicines can help prevent or reverse fat loss, like creatine, uridine and statins. The fact that there is not clinically proven therapy for patients with this essential problem, such as the slowness, with apparent absence of clinical recovery, makes the need for cosmetic surgical interventions (1).

Several forms of surgery have been used, with varying success, to repair body fat changes, like lipofilling, autologous free dermal fat graft, and others (7-11). In today’s busy and demanding world, we no longer have the luxury of taking weeks to recover. Therefore there is an urgent need to find a short solution to this facial correction.

An common strategy, at the moment, is to refill altered connective tissue matrices or subcutaneous tissue by injection of different agents (12). Injections into the facial tissue can help restore a more normal facial appearance by encouraging tissue growth and filling-out the sunken areas, but cannot regenerate facial cell.

Many different biomaterials with both bio-resorbable and no resorbable effect have been used for this purpose. These fillers should be biocompatible, non antigenic, easy to use, non migratory, either permanent or biodegradable, long-lasting, and natural-looking (13-14).

The most recent generation of filler materials includes injectable products based on polyacrylamide gels. Most of people have three to five sets of injections. Cheeks are normally spaced over six weeks.

Product

Water-based polyacrylamide gels represent a new generation of fillers. They are homogeneous
gels with viscosity and elasticity suitable for injection into soft tissues, thanks to the lack of particles and a very high concentration of water. Different subtype of polyacrilamide gel exist and have some history as a medical implant material (15).

Polyacrilamide hydrogel (PAIG) is a stable, atoxic, non-resorbable and sterile watery gel. It was employed for decades in the preparation of soft contact lents. In the last 15 years it’s been used in Russia and Ukraine in plastic and aesthetic surgery, for breast augmentation and facial correction, with very good results. At the present, it is widely used in biomedical research (as tissue implant, in detectors of penicillin antibodies, or as carriers of hormones and drugs in animal studies) as well as in industry. It has been used for soft tissue augmentation outside the United States since 1997. Despite some adverse events, the long duration of augmentation and the tangible filling effect has increased its use in Asia and in Middle East. It has been authorized for sale in Europe since March 2001 as a new medical device (CE-mark 0543).

Breiting et al in 2004 have conducted a retrospective study of 104 patients treated with PAIG injections for facial correction and they found excellent results (15).

In our study we used a PAIG formulation (*) that consists of approximately 2.5% to 5% cross-linked polyacrylamide and 97.5% to 95% non-pyrogenic water. Moreover, because of its relatively low cross-link density, it further contains many free ends that give the gel a constantly fluctuating molecular movement, that may reduce or prevent the settlement of biofilm, and then avoid the low-grade, long-term infection seen with other gels (this also explains why long-term adverse reactions have not been seen) (15).

Due to its unique characteristics the gel is highly bio-compatible: it does not cause any allergic reaction or any other immune effect either in animals or in humans. Since it is a non absorbable soft-tissue filler, it doesn’t migrate, but also its removal may be tricky, albeit possible. Hence the scope and targeting of the treatment should be precise, and the results considered permanent (15-19).

There are no reports of significant complications after injection of this material into face’s skin. Reactions to into-vessels injection of implant materials are rather uncommon, occurring locally, usually only in the early post-injection period (24).

Adverse reactions have been seldom described like cold abscesses and inflammatory superficial mini-nodules (25-28).

It is also reported that within 1-2 weeks after treatment the patient may develop transient oedema and tenderness at the treatment site (15-19).

Finally, there isn’t neither calcification nor cancer-causing effect (24).

It’s simple to use it; in addition, it needs no pretest. Standard precautions associated with the injection material should be followed. Obviously, when we perform injections on patients with low immune defence, like ours, complete antiseptic precautions and sterile conditions must be guaranteed.

The injection should not be made in or near skin areas with inflammation or an active skin disease. Polyacrylamide gel is not indicated for the treatment of fine wrinkles.

**OBJECTIVE**

This open-label study takes aim at the valuation of the efficacy and safety of facial injections of an Polyacrilamide Hydrogel (PAIG) in HIV-infected patients that showed different level (severe, moderate and mild) of facial lipoatrophy. Patients have to be informed about indications,
contraindications, expected results, precautions, warnings, and potential complications of the treatment.
As a matter of fact, they should be advised to avoid sunburn or frostbite in the area where polyacrilamide is injected.
Finally, they must sign an informed acceptance form provided by our team of experts.

MATERIALS AND METHODS
This was a randomized open-label study of PAIG’s injection in patients with HIV-related facial lipoatrophy (Table I).

| Table I  |
|-----------------|-------------------|
| **Subjects and their details and results** | **Mean ±DS** |
| Age (years) | 45.5 ± 6.4 |
| Mean duration of HIV (years) | 15 ±3.5 |
| Sex | |
| Female | 13 (36.2%) |
| Male | 23 (63.8%) |
| HIV transmission category | |
| IVDU | 9 (25.2 %) |
| Homosexual | 13 (36.2 %) |
| Heterosexual | 10 (27.5 %) |
| Other or unknown | 4 (11.3%) |
| CDC stage | |
| A | 11 (30.8%) |
| B | 14 (38.4%) |
| C | 11 (30.8%) |
| CD4 count(cells/µL) | 5705 (180-2113) |
| HIV viral load (copies/mL) | 24,900(<50-300000) |
| HBsAg positive | 9 (25.2 %) |
| HCV positive | 4 (11.3%) |
| Atrophy | |
| Mild | 12 (33.7%) |
| Moderate | 14 (38.5%) |
| Severe | 10 (27.8 %) |
| Previous treatment lines | 4 (1-9) |
| HAART duration (months) | 87.2 (21-130) |
We signed up to the study 36 patients in the aggregate. The majority of patients were male (70%) with mean duration of HIV years 15± 3.5. Every treatment consisted of the injection of 1 to 2 vials of PAIG on 0 day, and every 4 weeks for about 3 months, according to the level of facial lipoatrophy. If our patients had a mild lipoatrophy received four up to six vials, resolving their aesthetic facial modification.

The necessary amount of gel is injected in subcutaneous tissue, in a retrograde manner by injecting the gel while withdrawing the needle. After the injection a light manipulation helps to obtain an even distribution of the gel. Some patients develop pain only during the treatment. The injected gel will form a stable, soft part in the connective tissue.

Patient’s valuation has been done by facial eco­sonography, along with clinical examination. Withal we took standard photographs before and after the treatment, scheduled for successive 12th, 24th and 48th week.

The gel must be stored and protected from direct sunlight.

RESULTS

The cosmetic result was judged by patients and rated on an interval scale with four options ranging, from very good to very unsuccessful. All patients have been pleased with the aesthetic result, and they judged excellent elasticity and consistency in the treated area after 12 and 48 months.

In addiction, the skin sensitivity at the injection was assessed by a Pain-scale (from 0 to 10): a mean level of measured pain was 5 (±3). Long-term efficacy was assessed subjectively using Hospital Anxiety and Depression Scale (HADS) score (Table II).

All signs and symptoms which could possibly related to the injections has been taken into consideration, and we found that no serious complications and adverse effects were observed during the treatment: in most of case they were absent, and slight in the others.

Transient side effects, like swelling, reddening, itching or mild pain, may appear at the site of the intervention.

During the follow-up period we didn’t reported any long-term side effects with physical examination, that means to value signs by looking and palpating the skin: then we didn’t had neither migration of gel, palpable regional lymph nodes, scar tissue, pain at palpation, oedema or haematoma, nor hyperemia, wrinkles, peau d’orange, scratch marks, rash or polish-like skin.

The favourable trends in the efficacy of our results, noted at week 48 continued to the recall visit, as captured by subjective assessments of patients’ satisfaction with their facial appearance and diminished levels of anxiety and depression.

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<th>Table II</th>
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<td>Change from baseline in Hospital and Anxiety Scale scores</td>
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<td>Anxiety (mean, SD)</td>
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<td>Depression (mean, SD)</td>
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CONCLUSIONS

This study demonstrates that excellent results can be obtained using PAIG for the reconstruction of facial lipoatrophy (Fig 1-4). The filler has shown efficacy, tolerability and safety. In terms of aesthetic results, it makes a feature's improvement by giving an increased volume with a natural skin's viscosity and elasticity. The effect of tissue enhancement lasted over the entire study period. During the first year after treatment, no permanent soft-tissue reaction was observed. A volume reduction of about 10% occurs during the first 2 days as a consequence of an osmotic exchange between the sterile water content of polyacrylamide and the tissue fluid.

The benefit of non biodegradable hydrogel is that the augmentations are permanent, and no migration of the gel was detected in this material. We believe that both intermediate and long-term adverse reactions described in literature (like cold abscesses and inflammatory superficial mini-nodules) are caused by a bacterial low-grade infection, and that inherent characteristics of the implant determine the development of associated fibrosis (24).

![Fig. 1 Patient before treatment.](image1)
![Fig. 2 After 12 months' injections.](image2)
![Fig. 3 Young man forwards injections.](image3)
![Fig. 4 The same man at the end of 16 months' injections.](image4)
However, further studies, including long-term follow-up visits and cost-effectiveness evaluation are needed, along with critical analysis of results and a much longer time for definite conclusions. On the basis of our experiences with this promising material, we now prefer PAIG. Polyacrilamide gel so far is a promising material because of its easy use and harmlessness to the recipient (29, 30).
References


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