AQUAMID®

Four-Year Safety with Polyacrylamide Hydrogel to Correct Antiretroviral-Related Facial Lipoatrophy

Eugenia Negredo, Jordi Puig, David Aldea, Manual Medina, Carla Estany, Núria Pérez-Álvarez, Carmina Rodrígues-Fumaz, Jose A. Muñoz-Moreno, Carmen Higueras, Vicente Gonzales-Mestre and Bonaventura Clotet

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SUMMARY

- Four-year safety study at Germans Trias I Pujol Uni. Hospital in Barcelona, Spain.
- 145 HIV-infected patients were accessed following facial infiltrations with Aquamid between Sept. 2002 and April 2004.
- Patients presented with mild, moderate, severe and very severe facial lipoatrophy. The cumulative volume of Aquamid injected was 5.5 ml (4-18 ml pr. patient).
- Thus, large amounts of product can be used safely, and complications do not seem more likely to appear in other aesthetic enhancements using smaller volume.
- Only one patient presented with a local infection. Small palpable, non-visible nodules or indurations were the most frequent complication.
- Most patients (88.9%) were "satisfied" or very "satisfied" with the cosmetic results four years post infiltrations, because Aquamid looked and felt like normal tissue.
- Infiltrations with synthetic substances are effective strategies for repairing facial lipoatrophy.
- The high patient satisfaction and the low number of severe complications reflect the long-term safety of Aquamid for the repair of facial lipoatrophy.

BACKGROUND and INTRODUCTION

- Lipodystrophy may affect more than half the patients on long-term anti-retroviral therapy. Undoubtably, facial lipoatrophy is the most stigmatizing of these signs, and easily identifies a person as being HIV infected.
- Patients may suffer from psychological trauma, which can lead to delays in starting anti-retroviral therapy, treatment interruptions, or poor adherence with the possible risk of developing resistance.
- Though new treatments do not to the same degree cause lipoatrophy, successful solutions should still be offered to patients, who already show signs of these irreversible changes in body fat distribution.
- Infiltrations with polyacrylamide hydrogel is an effective strategy to revert anti-retroviral related facial lipoatrophy.
- Injectable polyacrylamide hydrogel (Aquamid®) is non-absorbable, homogeneous and particle-free consisting of 97,5% water and 2,5% cross-linked polyacrylamide.
- The authors:
  - evaluated efficacy and patient satisfaction in HIV+ patients injected with Aquamid.
  - determined long-term tolerance, durability and safety of Aquamid in HIV+ patients.

Study objective

The purpose of the study is to evaluate the long-term safety of polyacrylamide hydrogel (Aquamid) in human immunodeficiency virus (HIV) infected patients with facial lipoatrophy over a period of four years. Furthermore to determine patient satisfaction and the need for new infiltrations after initial treatment with polyacrylamide hydrogel.

Patients and Methods

This is a cross-sectional study including 145 HIV-patients, who received infiltrations with polyacrylamide hydrogel at Germans Trias i Pujol University Hospital in Barcelona, Spain. To assess the safety of polyacrylamide hydrogel more accurately, another 294 patients, who had received infiltrations although less than four years ago, were also evaluated. Subcutaneous infiltrations of polyacrylamide hydrogel were administered after anesthesia was given at the level of the infraorbital nerve. The quantity of substance depended on the severity of the lipoatrophy and the surgeon's evaluation. Further sessions of infiltrations were performed every three weeks, until the repair was considered successful.

Baseline Characteristics of Patients (N=145)	
Age (years)	47.2 (7.04)
Gender (men)	82.8
Time with HIV infections (years)	18.5 (4.1)
Risk behaviour, %	
Homosexual	42.1
Hetrosexual	23.8
Drug user	24.8
Time taking ARV therapy (years)	9.2 (4.9)
Time with facial lipoatrophy (years)	4.7 (0.57)
Severity of facial lipoatrophy, %	
Mild	6.2
Moderate	32.4
Severe	61.4
Injected volume of Aquamid (ml)	5.5 (4 - 18)

Epidemiological data, clinical data (HIV infection, severity of lipoatrophy, number of infiltrations, and complications), and psychological data (patient satisfaction) were collected from all patients as were facial photographs.

Clinical results and Discussion

Safety

During a mean of 50.2 (4.3) months after infiltration, only 1 of the 145 patients presented with a serious adverse event (local infection). Oral antibiotic was started 24h before and continued 15 days after the removal of the product with needle-aspiration, and the response was favorable and without sequelae.

Small palpable non-visible nodules (19.3%) and indurations (6.2%) were the most frequent complications observed. 53.6% were observed among patients with severe baseline facial lipoatrophy, whereas the rest affected patients with mild or moderate baseline atrophy.

Of the remaining patients (n=294), who also received polyacrylamide hydrogel for facial reconstruction but were not included in the current study, three presented a local infection in the infiltrated area making the overall incidence of facial infection 0.9% (4 out of 452). All patient responded well to treatment of the infection without sequelae except one patient in whom the infection occurred in the context of severe systemic infection.

Though all cases of infection involved patient with severe facial lipoatrophy, only small amount of product had been used. This supports the idea that infections are not necessarily associated with the amount of product injected, the sets of infiltrations administered, viral replication or immune status of the patient.

There were no reports of substance migration or problems with facial movements. The absence of animal protein in the product removes the risk of allergic reactions. The results indicate that infiltrations with Aquamid are a safe strategy for the repair of any degree of facial lipoatrophy

Patient satisfaction

Most patients (88.9%) were 'satisfied' or 'very satisfied' with the cosmetic results at least 4 years after infiltration, claiming that Aquamid looked and felt like normal tissue. More patients (92.7%) with mild to moderate baseline facial lipoatrophy were 'very satisfied' with the long-term results than those with severe lipoatrophy (86.5%).

The lower grade of satisfaction in subjects with severe baseline facial lipoatrophy stresses the need for earlier intervention to improve results and decrease the need for high quantities of product, and subsequently, the economic cost.

The filler works by adding volume from the gel itself, unlike other fillers, which need to produce an excessive foreign-body response to achieve the complete effect. Therefore, the aesthetic effect of Aquamid is immediate, predicting the results. And because the product is not absorbed, no periodic reinfiltration over time is necessary. This is also seen in the results, where only 17.4% of patients reported a mild impairment of facial lipoatrophy after the infiltrations. However, less than 9.2% of patients needed a new set of infiltrations after the initial set.

CONCLUSION

Four years after being injected with Aquamid most patients (88.9%) were either 'very satisfied' or 'satisfied' stating that Aquamid looked and felt like normal tissue. The rate of satisfied patients at four years follow-up was higher (92.7%) among patients with mild to moderate baseline facial lipoatrophy.

The very low number of major complications after at least 4 years of facials infiltrations with Aquamid reflect the long-term safety of this product for the repair of facial lipoatrophy. In addition, no periodic reinfiltration over time is necessary, because the product is not absorbed.

Complications related directly to the product seem very unlikely. Large amounts of product can be used safely, and complications do not seem more likely to appear than in other aesthetic enhancements, most of which involve smaller amounts of products.

CONTURA

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Contura is a medical technology company based in Denmark that develops and commercializes soft tissue fillers.

Contura's products – Aquamid® for facial contouring and Bulkamid® for the treatment of female urinary incontinence – are manufactured using the company's patented polyacrylamide hydrogel technology.

Aquamid is sold through a network of local distributors in 40 countries. Ethicon Inc., a Johnson & Johnson company, holds the exclusive worldwide distribution rights for Bulkamid, which is available in Europe.

Clinical trials evaluating Aquamid and Bulkamid are ongoing in the United States. Data from these trials will be used to support FDA applications for these products. Aquamid and Bulkamid are not approved for sale in the US.

Contura's products are developed, manufactured and tested in Denmark in compliance with the European regulatory requirements for medical devices.

AQUAMID

Aquamid® is a soft volume filler, which integrates with the body's own tissue and gives a natural look and feel. Produced using Contura's patented hydrogel technology, Aquamid is composed of app. 97.5% non-pyrogenic water and 2.5% cross-linked polyacrylamide and enjoys an unmatched track record of continuous high levels of patient satisfaction.

Aquamid was approved in Europe in 2001 and is available in 40 countries worldwide. Over 350,000 Aquamid infiltrations have been performed to date.

Science has always been the driving force behind Aquamid products. The efficacy and safety of Aquamid have been documented in more than a dozen clinical trials involving more than 5,000 patients. These studies have been published in peer-reviewed journals.

It is currently under clinical investigation in the U.S. for the aesthetic treatment of nasolabial folds. For more information please visit www.aquamid.com.

Contura International A/S · Sydmarken 23 · 2860 Soeborg · Denmark
Phone +45 39 58 59 60 · Fax +45 39 58 59 61 · info@contura.com · www.contura.com

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