A systematic review of filler agents for aesthetic treatment of HIV facial lipoatrophy (FLA)

Jared Jagdeo, MD, MS,[a,b,c] Derek Ho, BS,[a] Alex Lo, BS,[d] and Alastair Carruthers, MD, FRCPC, FAAD[e]
Mather and Sacramento, California; Brooklyn, New York; and Vancouver, British Columbia, Canada

HIV facial lipoatrophy (FLA) is characterized by facial volume loss. HIV FLA affects the facial contours of the cheeks, temples, and orbits, and is associated with social stigma. Although new highly active antiretroviral therapy medications are associated with less severe FLA, the prevalence of HIV FLA among treated individuals exceeds 50%. The goal of our systematic review is to examine published clinical studies involving the use of filler agents for aesthetic treatment of HIV FLA and to provide evidence-based recommendations based on published efficacy and safety data. A systematic review of the published literature was performed on July 1, 2015, on filler agents for aesthetic treatment of HIV FLA. Based on published studies, poly-L-lactic acid is the only filler agent with grade of recommendation: B. Other reviewed filler agents received grade of recommendation: C or D. Poly-L-lactic acid may be best for treatment over temples and cheeks, whereas calcium hydroxylapatite, with a Food and Drug Administration indication of subdermal implantation, may be best used deeply over bone for focal enhancement. Additional long-term randomized controlled trials are necessary to elucidate the advantages and disadvantages of fillers that have different biophysical properties, in conjunction with cost-effectiveness analysis, for treatment of HIV FLA. (J Am Acad Dermatol 2015;73:1040-54.)

Key words: facial volume loss; filler agent; highly active antiretroviral therapy; HIV facial lipoatrophy; HIV lipodystrophy; quality of life.

HIV facial lipoatrophy (FLA) is a subtype of HIV lipodystrophy associated with the use of highly active antiretroviral therapy (HAART),[1] and is characterized by facial volume loss that affects the contours of the cheeks, temples, and orbits. HIV FLA is socially stigmatizing and impacts patients' adherence to HAART,[2,3] psychological health, and quality of life (QoL), including feelings of distress, depression, anxiety, social isolation, and career barriers.[4]

HIV FLA has gained increased significance as patients have improved life expectancy with better medical management on HAART. Although new HAART medications are associated with less severe FLA, the prevalence of HIV FLA among treated individuals exceeds 50%.[5,6]

Filler agents are frequently used for treatment of HIV FLA to provide improvement in facial volume. There are limited published data on different filler options for treatment of HIV FLA with regards to out-of-pocket patient cost, required number of treatment visits, and filler longevity.[7] Treatment of HIV FLA is linked to improvement in the QoL of patients in categories including health perception, mental health,

From the Dermatology Service, Sacramento Department of Veterans Affairs Medical Center, Mather[a]; Department of Dermatology, University of California Davis, Sacramento[b]; Department of Dermatology, State University of New York Downstate Medical Center[c]; College of Medicine, State University of New York Downstate Medical Center[d]; and Department of Dermatology and Skin Science, University of British Columbia.[e]

Funding sources: None.

Disclosure: Dr Jagdeo is currently conducting an investigator-initiated study on HIV facial lipoatrophy (research grant) and is on the facial aesthetics advisory board (honoraria), Allergan Pharmaceuticals. Dr Carruthers has grant, research, and clinical trial support from Allergan Pharmaceuticals (onabotulinumtoxinA), Merz GmbH (incobotulinumtoxinA), and Revance Inc (RT 001 and RT 002). Dr Carruthers is a consultant and on advisory boards with Allergan Pharmaceuticals (onabotulinumtoxinA), Merz GmbH (incobotulinumtoxinA), Revance Inc (RT 001 and RT 002), and Kythera BioPharma. Jean Carruthers, MD (spouse) has grant, research, and clinical trial support; is a consultant; and is on advisory boards with Allergan Pharmaceuticals [neuromodulators and fillers (onabotulinumtoxinA)], Merz USA and Merz GmBH [neuromodulators and fillers (hyaluronic acid)], and Kythera BioPharma [sodium deoxycholate (deoxycholate)]. Authors Ho and Lo declared no conflicts of interest.

Accepted for publication August 19, 2015.

Reprint requests: Jared Jagdeo, MD, MS, Sacramento Department of Veterans Affairs Medical Center, Building 801, Dermatology Service, 10535 Hospital Way, Mather, CA 95655. E-mail: jrjagdeo@gmail.com.

Published online October 16, 2015.
0190-9622

http://dx.doi.org/10.1016/j.jaad.2015.08.040

social function, and emotional status.[8,9] Most published studies on the efficacy and safety of filler agents for treatment of HIV FLA have been observational studies. A grading criteria used for classification of HIV FLA severity, Carruthers Lipoatrophy Severity Scale, is also often used as a standardized measure to assess response of patients with HIV FLA to treatment with filler agents (Fig 1).[10]

The goal of our systematic review is to examine published clinical studies involving the use of filler agents for aesthetic treatment of HIV FLA and to provide evidence-based recommendations based on published efficacy and safety data.

CAPSULE SUMMARY

- HIV facial lipoatrophy is characterized by facial volume loss and is associated with social stigma.
- Based on published studies, poly-L-lactic acid is the only filler agent with grade of recommendation: B. Other reviewed filler agents received grade of recommendation: C or D.
- Filler agents are generally safe for aesthetic improvement of HIV facial lipoatrophy and improve patient quality of life.

METHODS

Search strategy and data extraction

A systematic review of the published literature was performed on July 1, 2015, on filler agents for aesthetic treatment of HIV FLA (please see Fig 2 and legend for detailed search strategy).

RESULTS

Study selection of filler agents for aesthetic treatment of HIV FLA

A total of 321 articles regarding the use of filler agents for treatment of HIV FLA were identified. After screening of titles, abstracts, and full text, 76 original articles were suitable in our review: poly-L-lactic acid (PLLA) (29), calcium hydroxylapatite (CaHA) (6), hyaluronic acid (HA) (7), polyacrylamide gel (PAAG) (9), polyalkylimide gel (PAIG) (11), polymethylmethacrylate (PMMA) (6), silicone oil (2), and autologous fat transfer (AFT) (6).

Articles were assigned a level of evidence (LOE) and graded according to the Oxford Center for Evidence-based Medicine LOE grades of recommendation (GOR)[11] (Table I). A list of filler agents used in published clinical studies for aesthetic treatment of HIV FLA can be found in Table II and detailed information on published clinical studies using filler agents for aesthetic treatment of HIV FLA can be found on http://www.jaad.org in Supplemental Table I.

Filler agents for aesthetic treatment of HIV FLA

Food and Drug Administration (FDA)-approved dermal fillers for treatment of HIV FLA are Sculptra (Galderma, Fort Worth, TX) (PLLA, 2004) and Radiesse (Merz Aesthetics, Franksville, WI) (CaHA, 2006). Clinicians have used the following filler agents off-label to treat HIV FLA: HA, PAAG, PAIG, PMMA, silicone oil, and AFT.

FDA approved for treatment of HIV FLA.

Poly-L-lactic acid

PLLA reconstituted in sterile water and lidocaine improves facial volume loss by serving as a scaffold, promoting fibroblast proliferation and neocollagenesis.[12] PLLA was FDA approved in 2004 as the first filler agent for treatment of HIV FLA.

An open-label, randomized study of either immediate or delayed PLLA treatment for HIV FLA was performed in 30 patients with HIV[13] (LOE 2b). Results at 12 weeks showed significant improvement in visual analog scale score for the immediate treatment group, and improvement in visual analog scale score was maintained from baseline in both treatment groups at 18 months[14] (LOE 2b). The most common delayed adverse event was injection-site nodules (31%).

A different open-label, randomized study of immediate or delayed PLLA treatment of HIV FLA evaluated 100 patients with HIV[15] (LOE 2b). By 24 weeks, patients with immediate treatment had significant improvement in FLA severity and QoL compared with patients with delayed treatment. At 48 weeks, there were significant changes of increased tissue depth measured by computed tomography imaging with subsequent 3-dimensional volumetric assessments at the maxillary, base of nasal septum, and mandibular regions for immediate treatment group patients[16] (LOE 2b). Subcutaneous nodules remained in 10% of patients at week 48.

Another open-label, randomized study of immediate or delayed PLLA or PAIG treatment of HIV FLA was performed in 134 patients with HIV[17] (LOE 2b). At 24 weeks, patients from the immediate treatment group had significantly lower FLA severity compared with patients in the delayed treatment group.

Twenty observational studies evaluated efficacy and safety of PLLA treatment for HIV FLA, and all studies reported positive outcomes for improving FLA severity and achieving high patient satisfaction[8,18-36] (LOE 4). Four case reports demonstrated PLLA treatment for HIV FLA improved FLA severity up to 24 months[37-40] (LOE 5).