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HIV facial lipodystrophy treatment by polylactic acid – a literature review

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Abstract

Human immunodeficiency virus (HIV) is a disease that negatively affects the immune system, requiring chronic, regular antiretroviral therapy, associated with numerous side effects. Lipodystrophy is one of them and is a serious clinical, psychological and social problem for patients affected by the problem. Volume loss and the formation of deep tissue defects in the facial area are caused by skeletal resorption and the redistribution of fat compartments, which progress with age but are also significantly exacerbated prematurely in the course of HIV and applied antiretroviral therapy. For a large group of patients, this constitutes a significant cosmetic defect, often leading to discontinuation of necessary, antiretroviral treatment. Various forms of treatment for this condition are currently available worldwide, including the implantation of non-permanent tissue fillers, such as hyaluronic acid-based fillers, or autologous fat cell transplants. The use of polylactic acid in the treatment of lipodystrophy is a therapeutic method with proven efficacy, effectiveness and a high safety profile, which will be discussed in this article.

Objective: A review of selected articles, literature, and the latest reports on the treatment of facial lipodystrophy associated with human immunodeficiency virus (HIV) using polylactic acid.

Material and methods: A review of the available literature from PubMed and Google Scholar, covering the years 2004–2024.

Conclusions: The treatment of HIV-related facial lipodystrophy with polylactic acid is a safe and well-tolerated method that provides long-lasting and satisfactory therapeutic outcomes, as confirmed by numerous scientific reports, as well as aesthetic results, supported by a high patient satisfaction rate. It is a minimally invasive procedure that can be repeated over time to maintain the desired aesthetic effect. This poses a challenge for physicians to optimise the therapeutic pathway for patients and refine procedural techniques. In this article, particular attention is drawn to the need for further research vis-à-vis the occurrence and treatment of potential early and late adverse effects following the use of polylactic acid. Emphasis is also placed on the possibility of expanding the group of patients eligible for the procedure, including pregnant women, those in the postpartum period, and minors dealing with HIV-related lipodystrophy.

Keywords: HIV facial lipoatrophy; HIV facial lipodystrophy; HIV, polylactic acid; facial volume loss

Human Immunodeficiency Virus (HIV) is the virus that causes Acquired Immunodeficiency Syndrome (AIDS). In the past, before the virus was isolated, researchers demonstrated that its mechanism of action is related to CD4 receptors on T lymphocytes. At the end of the 20th. century (1983), it was first isolated from a lymph node as a T-lymphotropic virus, which was later named Human Immunodeficiency Virus (HIV). This event marked the beginning of research on the virus and the disease it causes—acquired immunodeficiency syndrome (AIDS).

According to current knowledge, the mechanism of action involves the binding of the viral glycoprotein to the CD4 receptor on T lymphocytes, triggering a series of reactions at the nuclear and cytoplasmic levels, ultimately leading to the integration of the viral DNA into the host's chromosome. This ultimately results in the translation of the virus's genetic material and the formation of an infectious virion. HIV is divided into two subtypes: HIV-1 and HIV-2. HIV-1 is the most common variant and is associated with the occurrence of AIDS. [1][2].

HIV infection can occur through contact with the bodily fluids of an infected person, such as blood, semen, pre-ejaculate, vaginal secretions, rectal secretions, or breast milk. Some reports suggest the potential infectiousness of cerebrospinal fluid, synovial fluid, peritoneal fluid, or pericardial fluid; however, their infectivity is minimal. Saliva, sputum, sweat, tears, urine, faeces, and vomit that are not contaminated with blood do not pose a risk of infection. Infection requires contact of infectious material with damaged or intact mucous membranes, such as those of the vagina, rectum, oral cavity, or penis, damaged skin, or direct transfer into the bloodstream. [3][4]

The global number of people infected with HIV and those living with AIDS in 2019 was estimated at approximately 36.9 million. Currently, the number of new cases worldwide continues to rise. The highest regional concentration of HIV is found in countries of Central and Southern Africa. [5]

Lipodystrophy is a condition in which patients with HIV experience the loss of subcutaneous fat in various areas of the body. According to the publications gathered in this article, the most common areas affected by this disorder are the face, arms, thighs and buttocks. However, the problem of lipodystrophy can affect any area of the body. The occurrence of lipodystrophy in the facial area carries particular consequences, as the progressive, visible defect often leads patients to discontinue antiretroviral therapy due to the social impact and self-consciousness it causes.

Lipodystrophy can take 3 forms:

1) Lipoatrophy defined as the loss of subcutaneous fat.

2) Lipohypertrophy defined as excessive accumulation of adipose tissue.

3) Mixed form which is a combination of the two aforementioned disorders. The etiolopathogenesis and severity of the problem are multifactorial—ranging from the HIV infection itself, the duration of antiretroviral therapy and the medications used, comorbid conditions, genetic predispositions, to various environmental factors and lifestyle choices, such as diet, addictions and physical activity. Genetic factors, the patient's age or even ethnicity also have a significant impact. The exact mechanism of lipodystrophy associated with HIV infection remains not fully defined. According to the latest articles used in this work, one of the likely mechanisms of this disorder is the action of proteins produced by the virus, which, by interacting with the transcription factor PPARγ, inhibit the process of adipocyte differentiation. [6],[7],[8],[9],[10]

To date, objective and precise methods for classifying lipodystrophy have not been described in the literature. In a study published in 2009, the James Scale was used to classify facial lipoatrophy. This 4-point scale describes the issue based on its severity, relying primarily on the subjective perceptions of patients:

Stage I - mild form

Stage II - deeper atrophy with visible outline of facial muscles

Stage III - atrophy with clearly visible muscles Stage IV - the facial skin is directly on the muscles

Researchers are still working on a universal and objective classification that will clearly provide the means to assess the problem, its severity, and the extent of its progression. [11]

Polylactic acid and its mechanism of action Poly-L-lactic acid (PLLA) is a type of biodegradable, immunologically inert polymer with filling properties. It was approved by the U.S. Food and Drug Administration (FDA) for the treatment of HIV-related lipoatrophy in August 2004. Administration of the substance at the site of lipodystrophy increases tissue volume and fills tissue defects over time due to a local inflammatory response and stimulation

of type I collagen production. According to the latest reports, partial results are visible 4-6 weeks after the procedure, while complete results are typically seen after approximately 3-4 months and can last up to 2 years. There is an option to repeat the procedure according to the schedule planned by the physician. Poly-L-lactic acid is metabolised in the body to carbon dioxide and water. [12], [13], [14]

Patient Eligibility for the Procedure Using Poly-L-lactic Acid

In the studies reviewed, patients eligible for the procedure using poly-L-lactic acid were at least 18 years old and were HIV-positive. The severity of facial lipoatrophy induced by antiretroviral therapy ranged from 2 to 4 on the James Scale. The most common exclusion criteria were previous surgical interventions with fillers or inflammation in the facial area, use of nonsteroidal anti-inflammatory drugs within 7 days prior to injection, opportunistic infections, and pregnancy. [15], [16]

Aesthetic Outcome and Patient Satisfaction Following Therapy

In a series of observational studies assessing the aesthetic outcome and patient satisfaction with poly-L-lactic acid therapy and a significant improvement in the degree of facial fat atrophy was demonstrated. The procedures resulted in a high level of treatment satisfaction, as confirmed by patient satisfaction surveys, photographic documentation, three-dimensional laser scanning, and psychological questionnaires. [16], [17], [18], [19], [20]

Safety profile of the procedure and possible complications

Poly-L-lactic acid is characterised by a high safety profile when applied to the soft tissues of the face and body. It is important to remember that this substance is foreign to the body and may cause adverse effects both in its interaction with tissues and at the stage of application by the physician. According to the latest reports cited in this article, strict adherence to aseptic and antiseptic principles during the procedure is recommended, including the removal of any makeup from the patient's facial area beforehand. Additionally, cold compresses should be applied to the injection sites immediately after the procedure, and exposure to sunlight should be avoided. The use of poly-L-lactic acid in the area of the *orbicularis oris* muscle requires special caution, and it is categorically forbidden to inject it into the vermilion border. [12]

The most common adverse effects include localised swelling, nodules at the injection site, and tissue tenderness. Studies suggest that the formation of nodules may be influenced by improper

dilution of the product, incorrect injection technique, inadequate depth of injection, insufficient preparation time before administration, and facial muscle activity that results in the displacement of the product. Granulomas, which may develop secondary to the nodules, are the likely result of the patient's immune response (allergic or inflammatory reaction) and require treatment with local steroid therapy. Patients are also advised to perform massage for 5 days after the procedure, 5 times a day for 5 minutes each time. Local reactions in the form of erythema, swelling, and a feeling of warmth usually did not interfere with patients' daily functioning and typically resolved on their own. Persistent swelling or erythema require the inclusion of systemic steroid therapy, anti-inflammatory medications, and antihistamines. These reactions typically resolved within 7 to 10 days. The most severe and dangerous complication is localised skin necrosis, resulting from intravascular injection of PLLA—occlusion of the vessel lumen leads to impaired blood supply to the affected area of skin. To date, no substance has been identified that can effectively reverse the effects of intravascularly injected PLLA. To avoid this complication, it is important to administer small volumes of the product using a cannula, preferably with a linear retrograde technique, at the appropriate depth. Prior to injection, aspiration should be performed, and in case of vessel damage, warm compresses, topical nitroglycerin, and systemic steroid therapy should be recommended. [21] [22] [23]

According to the latest publications, PLLA may be subject to drug interactions. In patients taking anticoagulant or antiplatelet medications, the use of poly-L-lactic acid increases the likelihood of haematoma or active bleeding at the injection site. Anticoagulants should not be discontinued for the duration of the procedure.

In case of local infection, the use of alcohol-based antiseptics and chlorhexidine is recommended. [12]

To date, no studies have been conducted to evaluate the safety of using PLLA with other medications, fillers or anesthetics. Additionally, the safety and efficacy of PLLA use have not been evaluated in pregnant women, lactating women, or individuals under the age of 18. In elderly patients, after injecting the product into the deeper layers of the skin, the filling of existing wrinkles and improvement in skin elasticity were observed in the areas subjected to injection.

Discussion:

Numerous scientific reports indicate that the most critical area of the body for patients, in terms of aesthetics, psychology, social aspects, and functionality, that may exhibit features of lipodystrophy, is the face. Patients with facial lipodystrophy, due to HIV, experience significant discomfort and a decline in well-being, which often leads to discontinuation of antiretroviral therapy and increases the risk of mental health disorders, such as depression [24].

Based on the publications used in this article, researchers observed a clinically significant improvement in patients treated for lipodystrophy with poly-L-lactic acid.

Results from several years of observation in a group of 65 HIV-infected patients who underwent regular treatments (every 5 weeks) with PLLA until the desired aesthetic effect was achieved showed that patients with a higher degree of lipoatrophy on the James Scale needed more frequent treatments. In a patient with facial lipoatrophy at level I on the James Scale, the procedure needed to be repeated approximately every 21 months, whereas in a patient with facial lipoatrophy at level IV on the James Scale, the procedure needed to be repeated approximately every 13 months. After the study concluded, patients assessed the visual effect using a satisfaction questionnaire, achieving an average score of 4.9 (where 1 = very dissatisfied and 5 = very satisfied). [11].

According to a study by Cheryl M. Burgess and Rafaela M. Quiroga (2005), which evaluated the efficacy and safety of PLLA, after a 6-month observation period of a group of 6 patients with facial lipoatrophy infected with HIV, all reported complete satisfaction with the results of the treatment. On average, patients underwent 3 procedures during the 18-month observation period. Out of 61 patients, 48 required an average of 3 visits to achieve a satisfactory result, while the remaining 13 patients expressed a willingness to undergo additional PLLA treatments beyond the 3 procedures performed during the study. In 2 participants of the study, adverse effects manifested as palpable intradermal nodules, which resulted from localised accumulation of the administered substance and secondary proliferation at the injection site [25].

In addition to PLLA, other collagen-stimulating products such as calcium hydroxylapatite (CaHA) are used therapeutically for volumetric correction of the face exhibiting features of lipodystrophy. Scientists from the Icahn School of Medicine at Mount Sinai in New York (Leo van Rozelaar et al., 2014) conducted an observation study assessing the effects of poly-L-lactic acid administration using magnetic resonance imaging. The study involved 82 patients, with

observation spanning from May 2009 to September 2010. Among them, 41 patients were treated with PLLA, while the remaining patients received calcium hydroxylapatite (CaHA). In the group of patients treated with PLLA, an average of 5 procedures were performed (ranging from a minimum of 2 to a maximum of 7). Despite the fact that the amount of PLLA needed to achieve a similar aesthetic effect was significantly greater than that of CaHA, a lower incidence of complications was observed in the PLLA group (6 patients - 14.6%) compared to the CaHA group (8 patients - 19.5%). These were most commonly haematomas, nodules, and localised inflammation. The haematomas did not require intervention. In patients treated with CaHA, palpable nodules appeared, which were eventually subjected to surgical resection; this was not observed in the group of patients treated with PLLA. Inflammatory symptoms were treated with oral antibiotic therapy and it is suggested that this condition may have been related to improper dilution of poly-L-lactic acid (PLLA). Summing up the above study, despite noticeable side effects of the therapies used, there was a significant improvement in the self-esteem of all patients, due to the enhancement in facial appearance following treatment with poly-L-lactic acid (PLLA) and calcium hydroxylapatite (CaHA). It was observed that patients who received CaHA treatment achieved improvement in appearance in a shorter time, leading to a quicker enhancement in self-esteem compared to patients treated with PLLA. This may be related to the delayed final visual (volumetric) effect of PLLA compared to the nearly immediate visual effect observed after CaHA treatment. [15]

The procedure for administering PLLA to the facial area involves injecting an appropriate volume of the product subcutaneously or subperiosteally, most commonly using a fan technique, which allows more precise distribution of the product. For administering the medication, 26G injection needles are recommended. [15] The person performing the procedure is required to have specific and thorough knowledge of facial anatomy and physiology. Administering a poly-L-lactic acid-based product in an inappropriate area, using incorrect technique, or using an improper concentration can result in severe and long-lasting complications. Researchers agree in their publications that the procedure should be performed by qualified medical personnel, namely, a specialist in plastic surgery or a dermatologist, who has undergone appropriate training in administering poly-L-lactic acid to the facial area. Before the procedure, the doctor should properly qualify the patient and then discuss the potential outcomes of the procedure, including possible effects and complications that may arise from using the product. Patients should be advised against using dietary supplements and herbal products to avoid cross-reactions and unpredictable side effects. [12] [25]

The initial effect of "apparent fullness" after the procedure, disappears within about a week due to the gradual absorption of the solvent. Subsequently, the remaining PLLA molecules are surrounded by macrophages in response to the local inflammatory response and accumulation of the substance administered. According to the latest reports, redistribution of the administered preparation lasts up to 3 days. Due to its long half-life (approximately 6 months), PLLA is well-suited for the treatment of lipoatrophy, as its effects persist for several months. According to the latest publications, the effects can last from 12 to even 24 months. This allows the patient to fully experience satisfaction with the results without the need for frequent follow-up visits. [12] This treatment may require repetition, as PLLA is not a durable material. Its mechanism of action is not based on local stimulation of fat tissue growth but rather on increasing the thickness of the dermis. This effect results from the formation of new collagen fibres. [26] Nevertheless, a precise understanding of the mechanism of facial lipoatrophy in the context of HIV would provide researchers with greater opportunities to determine accurate dosages and treatment methods for lipoatrophy with specific preparations, including PLLA.

Conclusions:

Treatment of facial lipodystrophy in the context of HIV using polylactic acid is a safe and well-tolerated method that provides relatively long-lasting and satisfactory therapeutic outcomes, as confirmed by numerous scientific reports. It also delivers aesthetic benefits, supported by a high patient satisfaction rate, while maintaining a high safety profile with minimised side effects. It is a minimally invasive procedure that can be repeated over time to maintain the desired aesthetic effect, which presents a challenge for physicians to optimise the therapeutic pathway for eligible patients, as well as manage potential complications and expand the potential patient group dealing with HIV-associated lipodystrophy, who were previously excluded based on certain criteria.

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