

Oral Sensorimotor System in Patients with Facial Lipoatrophy Living with AIDS

ORIGINAL

Abstract

Introduction: Lipodystrophy Syndrome in people living with AIDS is characterized by body fat redistribution and metabolic abnormalities and is associated with the use of antiretroviral therapy (ART). It is socially and psychologically impacting once it reduces the quality of life of those who develop it. The prevalence varies from 6% to 69%.

Objective: Characterize the Oral Sensorimotor System in patients with Facial Lipoatrophy living with AIDS.

Methods: Cross-sectional convenience sample study. Sixty-four patients living with AIDS treated in the Lipodystrophy Clinic were clinically evaluated by the infectious disease physician and by the speech-language pathologist. The Oral Sensorimotor System structures were evaluated through the Orofacial Assessment Protocol.

Results: Changes in tone and mobility are associated with loss of subcutaneous fat.

Conclusions: Changes presented in the morphology and function of the Oral Sensorimotor System are associated with facial Lipoatrophy in patients living with AIDS.

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Keywords

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Introduction

The Lipodystrophy Syndrome (LDS) in individuals with the Human Immunodeficiency Virus (HIV) is characterized by body fat redistribution and metabolic abnormalities. Physically, there is lipoatrophy in peripheral areas such as the face, arms and legs and glutes and lipohypertrophy in central areas such as abdomen, mammary regions, and submental region and hump thus causing morphological changes in the human body [1].

This syndrome was formally described by the Food and Drug Administration (FDA) in 1997 [2] and given different names over the years, including "Crixbelly", "Pseudo Cushing's Syndrome", "Body Fat Redistribution Syndrome", "Metabolic Syndrome associated with ARVT" and "Dyslipidemic Lipodystrophy associated with HIV/ART"[3].

Initially, the syndrome was associated with the use of antiretroviral therapy (ART), in principle, to protease inhibitors (PI) and subsequently the use of inhibitors of reverse transcriptase nucleoside analogues (NRTIs), the latter category more associated facial lipoatrophy [4]. Later, it was observed that lipodystrophy also occurred in some patients who did not use ART, suggesting the involvement of other mechanisms, such as inflammatory factors, environmental and genetic factors. The fat tissue has an important contribution in the clinical and metabolic syndrome, since the mechanisms of differentiation of adipocytes are the main targets of action of antiretroviral drugs [5,6]. Treatment includes exchange of antiretroviral therapy (ART) and surgical procedures when possible to minimize volume changes in affected areas [6,7]. The pathogenesis of the syndrome remains unknown and its pathogenesis is probably multifactorial [8,9].

There is no consensus on the incidence of lipodystrophy in patients living with AIDS. Different studies suggest that this percentage can vary from 6 to 69% among patients with HIV in antiretroviral therapy for at least one year [10]. In Brazil, according to estimates by the Program on Sexually Transmitted

Diseases (STDs) and AIDS in the Ministry of Health-Brazil there are 600 000 people infected with HIV [11]. As for Facial Lipoatrophy no published an official estimate of the number of patients with this diagnosis.

In the face, lipodystrophy is characterized by loss of fat, especially in the regions of cheekbones (Bichat fat) and pre-temporal regions, which compose the Oral Sensorimotor System [12]. These alterations cause considerable psychological impact by giving the face a cadaveric aspect and revealing the diagnosis most patients wish to keep confidential [10-13]. The oral sensorimotor brings together several interconnected structures (lips, tongue, cheeks, teeth, soft and hard palate), with characteristics that develop common functions such as breathing, swallowing, chewing, sucking and speech and it is essential that this system is adequate in terms of morphology and functionality for the facial muscles to be healthy [14].

Orofacial Motricity can be defined as "the field of speech therapy focused on the study, research, prevention, assessment, diagnosis, development, habilitation, rehabilitation and improvement of the structural and functional aspects of orofacial and cervical regions" [15]. The speech therapy in the field of oral motor contributes to the stomatognathic balance and toning of the muscles of the face and neck, enabling better cosmetic results for patients [16]. Thus, the objective is to characterize the oral sensorimotor of Facial Lipodystrophy patients living with AIDS.

Methods

It is cross-sectional study of a convenience sample. Protocol was approved by the Ethics in Research of the Faculdade de Medicina do ABC (Case No. 360/2008) and conducted in a specialized clinic providing care to patients with HIV/AIDS of a Program for STD/AIDS and Viral Hepatitis of the Municipality of São Bernardo do Campo, São Paulo, Brazil, from

January to July 2009. The study included all patients referred to the Department of Speech Pathology during this period. There was no sample loss.

All patients were diagnosed with HIV/AIDS and facial lipoatrophy, had made use of Antiretroviral Therapy for a minimum of 12 months and aged over 18 years. Most had indication for facial filling with polymethylmethacrylate (PMMA) and met the criteria established by Ordinance No. 118 of 23 February 2005, of the Ministry of Health [17].

We used the sociodemographic and clinical aspects, obtained in a survey of medical records, to characterize a population: sex, age, ethnicity, duration of HIV diagnosis, use of ARVT and Facial Lipoatrophy; historical use of stavudine (D4T) and Efavirenz (EFV), being these antiretroviral drugs most commonly associated with the development of lipoatrophy in face; levels of CD4 lymphocyte count and serum viral load current, since these values are associated with the severity of lipoatrophy and are indicative of the clinical condition of the patient.

The total population consisted of sixty-four patients living with AIDS, clinically assessed by infectious disease physician for a diagnosis of Facial Lipoatrophy and assessed by speech therapy for evaluation of sensorimotor structures through the Oral Assessment Protocol Orofacial [18], that proposes to evaluate the morphology and function of the different components of the oral sensorymotor (face, lips, jaw, teeth, tongue, hard palate and soft palate) and assigns each item values from zero to one, according to the absence or presence of the item evaluated.

The data processing and analysis were performed by means of the software EPIINFO -A Word Processing, Database and Statistics Program for Public Health [19]- to prepare the database and the Statistical Package for Social Sciences-SPSS 17.0 for statistical analysis.

All findings with $p < 0.05$ were considered statistically significant. As a measure of risk, the adjusted

and unadjusted odds ratio, with their respective confidence intervals of 95% was calculated. We consider as the base category for each independent variable the odds ratio = 1, the lowest risk for the outcome of interest. Statistically significant variables in univariate analysis formed the model for multivariate analysis. Multiple logistic regression was used for the multivariate analysis.

Results

The sample consisted of 64 patients with facial lipoatrophy living with AIDS, mostly male (64.06%), Caucasian (95.31%) with a mean age of 48.9 years (predominantly in range between 38 and 47 years (standard deviation: 9.57). When evaluating the oral sensorimotor, we observed high frequency of changes regarding both the morphology of the face (100%) and the function (98.4%).

Discussion

Of all patients evaluated there was a predominance of males (64.06%) and Caucasian (95.31%) (**Table 1**). Although few studies relating exclusively to facial lipoatrophy, a study conducted in Spain involving sixty-two patients with this type of Lipoatrophy, showed a similar distribution, with 71% of male patients [20].

Males seem to be more prone to loss of fat in peripheral regions, while the female fat accumulates in the central regions [21]. Whereas facial lipoatrophy is a result of fat loss in peripheral regions, the number of males relative to females found in this sample probably arises from this factor.

The average age in this study was 48.9 years (range 36-73 years) (**Table 1**). The aforementioned work of Ribera et al, showed a similar average. In a comparative study of the volume deficit in the face of aging caused by changes in soft tissues and fat loss that occurs in lipoatrophy associated with HIV, it was found that this change, although it also

occurs, is lower in aging in relation to that occurs in persons with lipoatrophy [22].

Another recent report suggests that the progressive loss of facial fat, mainly because of the decrease of malar fat, causes skin grooves that cause wrinkling of the face [23] and the consequent appearance of more advanced age.

In Brazil there is a growing number of AIDS cases among individuals 50 years of age or older. Current

Table 1. Distribution of population by sex, age and ethnicity.

	N	%
Sex		
Female	23	35.94
Male	41	64.06
Total:	64	100.00
Race		
White	61	95.31
Black	1	1.56
Brown	2	3.13
Asian	0	0.00
Total:	64	100.00
Age		
18-27	0	0.00
28-37	6	9.37
38-47	28	43.75
48-57	21	32.81
58-67	5	7.81
68-75	4	6.25
Total	64	100.00
Source: Outpatient Program for AIDS Lipodystrophy in São Bernardo do Campo, São Paulo, Brazil		

estimates show growth in these cases, and among those over 60 years, the incidence rate reached 7.2 per 100 000 inhabitants in the year 2007 [24].

Publications related to senescence and senility patient's serum reagents are increasingly common. In 2006, UNAIDS reported that the seniority for these patients would begin at age 50 due to the difference between chronological age and somatic of approximately ten years. Although this fact is increasingly evident, the molecular basis of the aging process in these patients has not been completely elucidated [25].

The average age obtained in this sample, considering the publication of UNAIDS, makes us think that seniority, for these patients, can bring, besides all the health implications, deterioration of the appearance of the face as a result of Facial Lipoatrophy.

With the advances in AIDS treatment and reducing morbidity and mortality [26], there was an increase in life expectancy and, increasingly, we will have the combination of these two factors (age and lipoatrophy) directly interfering in facial contour of patients living with AIDS .

On average, patients had been diagnosed as HIV positive for 10.9 years (ranging from 11 to 22 years, had been using ARVT for 9.7 years (ranging from 10 to 20 years) and reported the first signs of facial lipoatrophy taking place 3.6 years before (**table 2**). Currently it is believed that HIV infection itself and not just the use of ARVT is associated with lipodystrophy and consequent insulin resistance and dyslipidemia [21].

Table 2. Descriptive measures of time of HIV diagnosis, use of ARVT, time of Facial Lipoatrophy and laboratory findings of patients with facial lipoatrophy living with AIDS.

	Average	Standard Deviation	Lowest Value	Biggest Value
Time of HIV diagnosis	10.9 years	4.2	2 years	22 years
Use of ARVT	9.7 years	3.5	1 year	20 years
Time of FacialLipoat.	3.6 years	2.4	1 year	10 years
T-CD4 Linphocites	659 cels/ml	352.5	1563 cels/ml	119 cels/ml
Viral load (detectable)	12143 copies/ml	19967.2	57843 cop/ml	56 cops/ml
Source: AIDS Lipodystrophy Outpatient Program in São Bernardo do Campo, São Paulo, Brasil.				

Considering that the facial lipoatrophy becomes more frequent the longer the period of use of ARVT, with demonstrably increased survival rates of these patients, the number of patients with facial lipoatrophy tends to increase [1, 28].

Thus, the patients in this sample associate two risk factors for facial lipoatrophy: prolonged periods of HIV infection and prolonged use of antiretroviral therapy.

The average count of CD4 T-lymphocytes was 659 cells/mL and the viral load was undetectable in 82.81% of patients (**Table 2**). The count of CD4 T cells is a predictor of opportunistic diseases and, therefore, a test of great value for the multidisciplinary team and patients.

The delay in the beginning of ARVT in asymptomatic patients with CD4 count around 350 cells/mm³ has been the strategy used in the clinic to decrease the time of exposure to these drugs and their adverse effects, since counting the very low CD4 initial is associated with increased risk of onset of lipodystrophy [26,28,29]. Currently, this strategy has been rethought, since this postponement could cause some harm to the patient and in several countries less than 500 CD4 cells/mm³ are already considered as evidence of the need to start ARVT.

The chronic inflammation caused by infection by HIV has also affected the criteria for initiation of treatment. Even in patients with favorable ratios of CD4 and Viral Load it has been observed that the HIV virus leads to the deterioration of different organs and tissues of the body [30]. Anticipating the onset of the antiretroviral therapy will also increase the time of exposure of patients living with AIDS to these drugs in the course of their lives.

In this sample, 100% made use of antiretroviral therapy for a year or more, and the average use time was of 9.6 years (range 2-20 years). The Stavudine (D4T) was used by 87.5% of patients and Efavirenz (EFV) by 76.56% of them. The use of two antiretroviral was made by 68,75% of the patients.

Several studies have associated the use of Stavudine to the occurrence of lipodystrophy and more specifically to Facial Lipoatrophy [10, 20, 31, 32, 33]. Recent studies have demonstrated that Efavirenz is also associated with the onset and progression of lipoatrophy [5]. Although in small quantity (4.69%) there are patients who had never made use of D4T and EFV who developed Facial lipoatrophy, which corroborates the likelihood of Lipodystrophy being a multifactorial syndrome.

While medication (ART) is critical to ensure the survival of patients, this turned AIDS into a chronic disease. Its use can accelerate the development of facial lipoatrophy, negatively affecting the quality of life of those who develop it [34].

It is believed that the combination of such factors as the use of Stavudine (D4T), weight loss greater than 7 kg and a long period of HIV infection significantly increase the risk of developing lipoatrophy and the longer the duration of use of ART, the greater the likelihood of developing it [27]. Weight loss is a common fact in the history of patients living with AIDS, especially in the early stages of the disease, and is often the reason to verify the presence of HIV. Also common are weight changes in the presence of opportunistic diseases.

Many patients on developing the Facial Lipoatrophy tend to reduce adherence to treatment or suggest the possibility of changing the therapeutic regimen. However, it is already established that the change of medication, when possible, despite reducing lipid abnormalities, scarcely provide improvement of the condition [31, 35].

Studies of switch, which proposed to evaluate the exchange of antiretroviral drugs as a means to decrease toxicity did not have a consensus. The improvement depends on a number of variables, including severity of lipoatrophy at the time of replacement, the duration of drug use, follow-up and the monitoring of the underlying HIV infection. Furthermore, they can lead to failures and viral drug resistance [36].

The patients in this sample made use of various therapeutic regimens in treatment evolution, not only in order to follow the changes in the guidelines proposed by the Ministry of Health of Brazil, but mainly because of virological failure, maladaptation the medication or as a result of adverse effects presented.

In Brazil, stavudine (D4T) was liberated for use in 1994 and Efavirenz (EFV) in 1998, with approximately 15 years of medication use by patients. Efavirenz is still a drug of first choice in the composition of the initial therapeutic regimen of patients. In the past, with few drugs available in the market, they were widely used medications and their side effects, have only recently been demonstrated, especially in relation to D4T, which currently has a very limited indication.

In general, changes in face were perceived by the patient (84.37%) and it is he who feels the discomfort related to this change (82.81%). Even in cases where the perception of facial changes was reported by the physician or by the spouse,

the patient was able to perceive a difference in the face after oral myofunctional exercises / or facial filling.

There are published reports that 28.3% of patients on ART are afraid of developing facial lipoatrophy [37]. Self referral for a professional to assess the face and discard the possible diagnosis of Facial lipoatrophy is becoming more frequent. It is also common for patients to consult several specialists from different areas (infectious diseases, plastic surgery, speech therapy and psychology) to make sure they do not have lipoatrofia/lipohypertrophy or that, when present, is not evolving.

Thus, the discomfort and the implications of Facial Lipoatrophy go beyond aesthetics. They're intrinsically related to disclosure of diagnosis (85.93% did not reveal their diagnosis), this is probably one of the reasons why the percentage of patients who say they are uncomfortable with the change in the face is so high (**Table 4**).

Another probable reason is that the change in the face cause degradation of body image, leading

Table 3. Morphology Characterization of sensorimotor Oral and statistical analysis.

Structure Evaluated	Expected Score	Patients with abnormalities	%	P Value	Odds Ratio	IC 95%	Response Proportion	IC 95%
Face	02	3	4.7	1.0000	1.049	0.1432-7.688		
Lips	03	9	14.1	1.0000	1.164	0.2255-6.003		
Tongue	04	0	0	1.0000	1.0000	0.2396-4.174		
Dentition	04	63	98.4	0.0003	64	5.728-715.1		
Superior	01	58	90.6				0.752256	0.589103-0.865426
Inferior	01	60	93.7				0.752256	0.589103-0.865426
Dental Occlusion	03	23	35.9	0.6798	1.561	0.3004-8.112		
Hard palate	04	52	81.2	0.0395	5.333	1.170-24.32		
Incisor papilla	01	52	81.2				0.997113	1.94E [10]-1
Soft Palate	04	9	14.1	1.0000	1.164	0.2778-4874		
Total	24	64	100					

Source: Outpatient Program for AIDS Lipodystrophy in São Bernardo do Campo, São Paulo, Brazil.

to emotional and sexual difficulties [38]. The face is socially considered the "business card" of the individual and an appearance which differs from the commonly accepted causes social implications stressful for patients, because of the prejudice associated with the disease.

A recent study published by the Center for AIDS and STD Research - USA showed that there is a close correlation between changes in body composition of patients living with AIDS and depression and the facial lipoatrophy was considered the most critical because it was responsible for more severe degrees of depressions [21]. The association of the use of psychotropic medications and ARV by patients living with AIDS is increasingly frequent.

For this reason, to characterize the SSMO of these patients and to define strategies to adapt it is essential to ensure adherence to treatment and help in improving the quality of life of people living with AIDS.

In the evaluation of patients with facial lipoatrophy living with AIDS, there was a high frequency of changes regarding both the morphology of the face (100%, $P = 0.004$), and the function (98.4%, $P < 0.0001$) (tables 3 and 4). Regarding morphology, no patient achieved expected total score.

The areas with the highest rates of alteration were dentition ($P = 0.0003$), characterized by partial or total absence of teeth in 98.4%, changes in

the conformation of the hard palate ($P = 0.0395$), characterized by hypertrophy of the incisive papilla (81.2%) and changes in side dental occlusion, characterized by the absence of "molar switch" (35.9%). Changes in lips (upper) and soft palate (tonsils) occurred in a smaller portion of the sample (14.1%). The morphology of the tongue area showed no change (Table 3).

The absence of teeth and changes in the dental arch, mainly at the molars and premolars associated with the loss of fat in the face, significantly compromise the appearance of such patients, since without this bulkhead, there is a greater depression of the face. Patients living with AIDS and antiretroviral therapy for more than 1 year, with changes in the dentition are 64 times more likely to develop Facial Lipoatrophy.

The high incidence of change of the hard palate is related to hypertrophy of the the incisive papilla and associated with poor posture of the tongue at rest that, in general, in these patients were improperly positioned at the oral cavity floor, when the proper would be the dorsum of the tongue gently touching the hard palate and delicately the tip in contact with the alveolar ridge, filling the cavity of the mouth. It is noteworthy that the changes of the hard palate, on this population using HAART, adds a 5.33 times greater risk of facial lipoatrophy.

The other anatomically altered areas interfere with performance, ie the function.

Table 4. Function of oral sensorimotor and statistical analysis.

Structure Evaluated	Expected Score	Patients with abnormalities	%	P Value	Odds Ratio	IC 95%	Response Proportion	IC 95%
Face	09	56	87.5	0.0007	8	2.456-26.06	0.489394	0.317727-0.6636
Lips	09	39	60.9	0.0952	2.56	0.9109-7.195		
Jaw	08	31	48.4	0.2653	1.939	0.6676-5.634		
Tongue	13	51	76.7	0.0015	4.923	1.860-13.03	0.597028	0.354747-0.799702
Soft Palate	05	0	0	1.0000	1.0000	0.2760-3.623		
Total	44	63	98.4					

Source: Outpatient Program for AIDS Lipodystrophy in São Bernardo do Campo, São Paulo, Brazil.

The area with the highest rates of change was the face ($P = 0.0007$), being the nasolabial groove and labiomarginal the evaluated areas with higher rates of impairment (87.5%), these areas are often where there is loss of subcutaneous fat in patients with facial lipoatrophy.

As these areas are also affected by advancing years, it is often difficult to differentiate the cause of this change (lipoatrophy or aging) and what the most appropriate treatment for their fix is, even for experienced professionals in this area. Changes in function of face mean 8 times more chances of developing facial lipoatrophy.

The alteration in posture of the tongue ($P = 0.0015$), which appeared positioned in the oral cavity floor or between the dental arches in 79.7% of patients, besides compromising the morphology of the hard palate, is also often associated with orthodontic with alterations, which were also frequent in the study population. Patients living with AIDS on ART for more than one year and with alterations in the function of the tongue are 4.92 times more likely to develop facial lipoatrophy.

The difficulty in lateralization of lips, observed in 60.9%, is probably associated with the loss of fat in the malar and preauricular region. The function area of the soft palate had no alteration, despite the high frequency of absence of tonsils, identified as change in morphology of the soft palate (**Table 4**).

In the only study related to speech therapy in patients with AIDS found, this was related to changes in the articulation of phonemes, speech or swallowing, due to clinical manifestations in the oral cavity, such as candidiasis, aphthous ulcerations in the hard and soft palates, angular cheilitis papillomas in the posterior wall of the pharynx and larynx or herpes zoster affecting the hypoglossal nerve [39].

These alterations are still affected patients with HIV, particularly in the acute phase of the disease. It is often from the recurrent appearance of

such that serology for detection of anti-bodies is requested.

It is not surprising that in the study mentioned above no cases of Facial lipoatrophy had been reported. The first ordinances of the Ministry of Health of Brazil, in that regard date back to 2004, after which professionals and patients started paying more attention to this alteration. In analyzing the records of this sample were also not found notes referring to the loss of subcutaneous fat in prior to this date.

It was only from 2006 onwards that we started to consider the importance of observing the patterns of chewing and swallowing of these patients [23], probably not because of their relation with facial lipoatrophy alterations, but because of dysphagia and microaspirations that caused pneumonia applicants already in immunodepressed patients and further reduced their survival.

Thus, the unfamiliarity in the area of infectious disease and short survival of these patients in the past, after the diagnosis of HIV or AIDS appear to be a causal factor for the the lack of information in the literature of interventional procedures in the field of speech in this particular population.

Alterations in morphology, for the most part, can be minimized or corrected with prosthetic or therapeutic interventions. However, in São Bernardo do Campo, at the time of data collection, there was no service that would guarantee, using the public health system, prosthodontic treatment for these patients, who often stood with missing teeth or ill-fitting and old dentures.

Functional alterations benefit from myofunctional oral exercises, when carried out with periodicity which can improve the appearance of the face and minimize the consequences of facial lipoatrophy. In studies unrelated to patients living with AIDS, there is evidence that after traditional oral myofunctional speech therapy, there are significant results of im-

provement in the quality of symmetry, morphology, physiology and muscle tone [40].

Since Facial lipoatrophy has no cure, the Ministry of Health of Brazil makes available, through the National Health System, surgical procedures for filling in the areas with cutaneous atrophy, aiming to tackle the stigma caused by it. This is because the treatment of facial lipoatrophy improves the psychological state, enhances the quality of life and promotes adherence to ART, which is the biggest concern of the multidisciplinary team treating the patient [41].

Currently the methods of restoration of facial volume include the use of substances such as polymethylmethacrylate (PMMA) [42], a product approved by the Ministry of Health of Brazil. Its use, however, has limitations, even though it is the only filler approved for use in patients with AIDS.

The absence of an ideal strategy for treating these patients is consensus in the medical literature since they all have some contraindications and may cause adverse effects even considering the inclusion and exclusion criteria [43]. There are several references on such limitations involving the different strategies available to combat this syndrome and therefore there is a need to explore alternative options for action [44].

Although the facial filling is the most appropriate strategy to improve short-term appearance of the patient, many times they do not meet the clinical criteria for the procedure to be performed. For this reason, in 2009, in a pioneering way, the Ministry of Health of Brazil recommended in its publications, the "exercises of the muscles of mimicry (facial gymnastics)" considering they can "mitigate and restore aesthetic balance of the face" [5], which confirms the importance and necessity of characterizing the oral sensorimotor of these patients, in order to establish the best treatment plan for rehabilitation [45, 46].

In conclusion, the assessment of oral sensorimotor of patients in this study indicated alterations in

tone and mobility associated with loss of subcutaneous fat, factors which contribute significantly to the deterioration of physical appearance. This medical condition results in impairment of social interaction, for the subjective feeling that their appearance is indicative of the diagnosis of AIDS.

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