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Lipodystrophy in children and adolescents with acquired immunodeficiency syndrome and its relationship with the antiretroviral therapy employed

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Abstract

Objective: To evaluate the presence of clinical lipodystrophy in children with the acquired immunodeficiency syndrome and to relate it to the antiretroviral regimen employed, to changes in lipid profile and to insulin resistance.

Methods: This was a cross-sectional study that evaluated 30 children and adolescents (median age = 9.1 years) with the acquired immunodeficiency syndrome during 2004 and 2005. The following clinical and laboratory evaluations were performed: classification of HIV infection, anthropometric measurements (weight and height), serum glycemia, serum insulin and lipid profile (LDL-c, HDL-c, triglycerides). Lipodystrophy was diagnosed using clinical parameters. The chi-square test was used for statistical analysis.

Results: All of the patients were taking antiretroviral therapy regularly (median duration of 28.4 months); 80% were on three drugs in combination (highly active therapy) and 30% were on protease inhibitors. Lipodystrophy and dyslipidemia were observed in 53.3 and 60% of the patients, respectively. Children on a highly active therapy regimen with protease inhibitors exhibited a higher percentage of mixed lipodystrophy; the difference between these children and the group on highly active therapy without protease inhibitors and the group not on a highly active therapy was statistically significant (44.4 vs. 16.7%; p = 0.004). There was no statistically significant association between the presence of lipodystrophy and sex, age (> 10 years), changes to the lipid profile or insulin resistance.

Conclusions: The elevated prevalence of dyslipidemia and lipodystrophy observed among children with acquired immunodeficiency syndrome, which exhibited a relationship with the antiretroviral regimen employed, may represent an increased risk for future complications, in particular cardiovascular problems.

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Introduction

Advances in the treatment of children with acquired immunodeficiency syndrome (AIDS), including the use of highly active antiretroviral therapy (HAART) have made it possible to achieve significant suppression of viral replication with consequent reductions in morbidity and mortality and improvements in patient quality of life. Currently, HAART is recommended for the initial treatment of HIV infections in children.[1] However, these drugs have been linked with the

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development of metabolic abnormalities that in conjunction are known as HIV lipodystrophy syndrome and which are characterized by increased plasma levels of atherogenic lipoproteins, insulin resistance, diabetes and redistribution of body fat in both adults and children.[2,3]

Lipid abnormalities associated with the use of antiretroviral drugs are common and are most strongly related to treatment with ritonavir, efavirenz and d4T.[2,4] Insulin resistance has also been found in 8 to 10% of adult patients with AIDS.[5] The presence of lipid and glucose metabolism abnormalities may lead to an increased risk for the development of noninfectious chronic diseases, such as atherosclerotic disease, which begins during childhood.[6]

Another adverse event related to the increased cardiovascular risk resulting from the use of antiretroviral therapy is mitochondrial toxicity, which leads to an increase in production of reactive oxygen species, resulting in exacerbation of oxidative stress, especially when accompanied by compromised antioxidant defense.[7]

From 20 to 50% of children with AIDS treated with HAART, including protease inhibitors, develop dyslipidemia(s), the most common of which is elevated total cholesterol and LDL.[8] In adults with HIV, dyslipidemia is associated with an increased risk of developing cardiovascular diseases. There is no consensus on the treatment for dyslipidemia(s) in children with AIDS. However, it is worthy of note that treatment with statins, especially in high doses, in association with protease inhibitors, increases the risk of myositis/myolysis.[8]

With relation to the lipodystrophy syndrome, studies indicate that the prevalence is 25 to 30% among the pediatric population with AIDS and that the mean time taken for abnormalities to appear after starting HAART is between 7 and 31 months. Clinical diagnosis of lipodystrophy, widely used in practice, underestimates the redistribution of body fat when compared with specific tests for the same purpose, such as dual-energy X-rays (DXA).[9]

There have been few studies evaluating the relationship between redistribution of body fat assessed clinically (lipodystrophy) and lipid and glucose metabolism abnormalities in children with AIDS. It is against this background that this study was carried out with the objective of evaluating the presence of clinical lipodystrophy in children with AIDS and relating it to their antiretroviral regimens, lipid profile abnormalities and insulin resistance.

Methods

This was a cross-sectional study carried out in 2004 and 2005, with 30 children and adolescents with AIDS, of both sexes, aged 4 to 14 years and being seen regularly at the Pediatric Infectology Clinic at the Faculdade de Medicina do ABC (FMABC) in Santo André, SP, Brazil and at the São Bernardo do Campo Referral Center, SP, Brazil. The study was approved by the Research Ethics Committees at the FMABC and the Universidade Federal de São Paulo, and prior written consent was obtained from patients' parents or guardians. The protocol being used to treat HIV infection was that proposed by the Centers for Disease Control and Prevention.[10]

Children and adolescents were excluded if they were on corticosteroids, if they had suffered severe disease or been admitted to hospital during the 3 months prior to starting the study or if they had other chronic diseases such as heart disease, kidney disease, neuropathy, rheumatic diseases, lung disease or liver disease.

At the time that the study was carried out, there were 38 patients with AIDS being treated at the two services named above and who met the inclusion criteria and did not present any of the exclusion criteria; seven parents or guardians either did not give consent or did not attend after three invitations and one adolescent was excluded after chronic lung disease was detected.

A standardized questionnaire was administered to the group of AIDS patients, collecting data on identification, type of transmission, prophylaxis, breastfeeding, age at diagnosis of infection, regimen and duration of antiretroviral therapy at time of enrollment on the study, viral load and CD4 count (taken at a maximum of 3 months before or after the study outset).

Socioeconomic assessments were made using the Brazilian Economic Classification Criteria (Critério de Classificação Econômica Brasil), which is based on family spending power and the head of the family's level of education.[11] The patients' living conditions and environment were also taken into account.[12]

Anthropometric measurements (weight, height) and classification of nutritional status were carried out in accordance with World Health Organization recommendations.[13] Therefore, malnutrition and/or short stature were defined as a z score ≤ 2 for body mass index and/or height/age.[14]

Puberty staging was carried out by a single pediatrician using the criteria proposed by Marshall & Tanner for both sexes (breasts and testicular development).[15]

A diagnosis of clinical lipodystrophy was made when two independent examiners detected either lipoatrophy (reduced fat in peripheral areas, such as arms, legs and buttocks, and relatively prominent muscles and veins), lipohypertrophy (accumulation of fat in the abdominal region, dorsal gibbosity, gynecomastia and increased breast size in adolescents/females) or a combination of lipoatrophy and lipohypertrophy.[16]

Peripheral venipuncture was used to collect 10 mL of blood from each patient after 12 hours' fasting in order to assay the following:

- Lipid profile, using the BioExpress Plus (Bayer) enzymatic-colorimetric kit. Triglycerides, HDL-c and LDL-c were classified according to the cutoff points proposed by the National Cholesterol Education Program.[17]
- Serum insulin, with the IMMULITE chemiluminescence insulin kit (DPC MedLab).
- Serum glycemia, using the BioExpress Plus (Bayer) enzymatic-colorimetric kit.

Insulin and glycemia results were used to calculate the homeostasis model assessment (HOMA-IR), with insulin resistance defined as HOMA-IR > 3.0.[18]

The Statistical Package for the Social Sciences (SPSS) version 13.0 was used for statistical analysis.[19] Anthropometric indicators were calculated using the software program Epi-Info 2000 version 3.3.2.[20] frequency tables were used to describe categorical and bivariate variables and the chi-square test was used to evaluate differences between percentages of abnormal test results for categorical variables. The significance cutoff adopted was $\alpha < 0.05$.

Results

Table 1 contains the general characteristics of the 30 children and adolescents with AIDS enrolled on the study. Fourteen (46.7%) of them were male and the mean age was 9.1 years (±2.5 years). The majority of them were prepubescent (n = 22, 73.3%) and the most common socioeconomic class was C (n = 18, 60%). With relation to nutritional status, four (13.3%) of the children and adolescents with AIDS had a z score of < -2 for weight/height, four (13.3%) for height/age and one (3.3%) for the ratio between weight/height and height/age.

All of the children and adolescents with AIDS contracted the infection by vertical transmission. Twenty-seven (90%) of them did not receive any type of prophylaxis and 24 (84%) were breastfed. The median age of the children and adolescents at diagnosis of AIDS was 4.5 years (minimum-maximum: 2-12 years) and the most frequent diagnosis stage was B1 (n = 13, 43.3%). The median time on the regimen in use at study outset was 28.4 months (minimum-maximum: 7.0-85.2). Twenty-four of the 30 (80%) patients were on three drugs in combination, and nine (30%) were taking at least one protease inhibitor (Table 2). All of the children taking protease inhibitors were also on HAART. Table 2 provides details on the antiretroviral therapies the children and adolescents were on together with presence/absence and type of lipodystrophy.

With relation to the lipid profile, 18 (60%) of the children and adolescents with AIDS exhibited some type of abnormality. Abnormal LDL-c, HDL-c and triglycerides

Table 1 - Characterization of the children with acquired immunodeficiency syndrome (n = 30)

Variables studied	n (%)
Classification of HIV infection	
A2	7 (23.3)
A3	1 (3.3)
B1	13 (43.3)
B2	6 (20)
B3	3 (10)
CD4 count*	749 cells/mm^3 (349-1,781)
Viral load*	200 x 10^3 copies/mm^3 (172 x 10^3-533 x 10^3)
Time on current antiretroviral regimen*	28.4 months (7.0-85.2)
Medications	
NRTI	30 (100)
NNRTI	15 (50)
PI	9 (30)
Treatment regimens employed	
NRTI + NRTI	6 (20)
NRTI + NRTI + NRTI	1 (3.3)
NRTI + NRTI + NNRTI	14 (46.7)
NRTI + NRTI + PI	8 (27.7)
NRTI + NNRTI + PI	1 (3.3)

NNRTI = non-nucleoside reverse transcriptase; NRTI = nucleoside analog reverse transcriptase inhibitors; PI = protease inhibitors.
* Median and minimum-maximum.

Table 2 - Breakdown of antiretroviral drugs and variables associated with lipodystrophy

Patient	Sex	Age (years)	Stage	Drug 1	Drug 2	Drug 3	DIAG	TOR (months)	Lipodystrophy	↑ LDL-c	↓ HDL-c	↑ TG	IR	EPM	SS
1	M	8.2	B2	AZT	ddI	NFV	6.0	30.4	None	-	-	+	-	-	-
2	F	9.6	B1	AZT	ddI	-	4.0	44.6	Lipohypertrophy	-	-	-	-	-	-
3	F	6.7	B1	AZT	3TC	EFZ	2.0	30.4	None	-	+	-	-	-	-
4	F	10.5	A2	AZT	ddI	NVP	4.0	20.3	Lipohypertrophy	-	-	+	-	+	-
5	F	13.6	B3	d4T	3TC	EFZ	6.0	7.1	Lipohypertrophy	-	-	-	-	-	-
6	M	7.1	B1	AZT	ddI	NFV	4.0	30.4	Mixed form	-	-	-	-	-	-
7	M	11.2	A2	AZT	ddI	NFV	7.0	31.4	Lipohypertrophy	+	-	+	-	-	-
8	M	9.3	B1	AZT	ddI	EFZ	2.0	58.8	None	+	-	-	-	-	-
9	M	5.1	B1	AZT	3TC	ABC	2.0	13.1	Lipohypertrophy	-	+	-	-	-	-
10	F	13.5	B3	AZT	ddI	EFZ	12.0	15.2	Lipohypertrophy	-	+	+	-	-	-
11	M	10.8	A2	d4T	EFZ	LPV/r	2.0	7.0	Mixed form	-	-	-	-	-	-
12	F	10.1	B1	3TC	ddI	LPV/r	3.0	26.3	None	-	-	-	-	-	-
13	F	7.2	B1	d4T	ddI	RTV	2.0	38.5	None	-	-	+	-	+	-
14	M	10.8	A2	AZT	3TC	NVP	7.0	18.2	None	-	-	-	+	-	-
15	F	10.7	B2	AZT	ddI	-	3.0	64.9	Lipohypertrophy	-	-	-	-	-	-
16	M	7.6	B1	AZT	ddI	-	4.0	30.4	Lipohypertrophy	-	-	-	-	-	-
17	F	7.1	B2	AZT	3TC	EFZ	2.0	32.4	None	+	-	-	-	-	-
18	M	8.8	B2	AZT	ddI	NVP	2.0	85.2	None	-	-	+	-	+	-
19	M	9.4	A2	AZT	3TC	-	6.0	24.3	None	-	-	-	-	-	-
20	M	7.2	A2	AZT	3TC	NVP	6.0	17.2	None	-	-	-	-	-	-
21	F	6.2	B2	AZT	ddI	EFZ	2.0	7.2	Lipohypertrophy	-	-	-	-	-	-
22	M	7.0	A3	AZT	3TC	EFZ	3.0	31.4	Lipohypertrophy	+	-	-	-	-	-
23	M	3.9	B1	AZT	ddI	NVP	2.0	45.6	None	-	-	-	-	+	-
24	F	12.0	B3	AZT	3TC	EFZ	5.0	13.1	Lipohypertrophy	-	-	-	-	-	-
25	F	11.2	B2	AZT	ddI	NVP	8.0	25.3	None	+	-	-	-	-	-
26	M	14.0	B1	d4T	ddI	NFV	5.0	7.1	Mixed form	-	-	-	-	+	-
27	F	6.0	B1	3TC	d4T	NFV	2.0	7.0	Mixed form	+	-	-	-	-	-
28	F	8.2	B1	AZT	3TC	-	2.0	70.0	None	-	-	-	-	-	-
29	F	10.1	A2	AZT	ddI	-	2.0	53.7	None	-	+	-	-	-	-
30	F	9.8	B1	AZT	ddI	NFV	4.0	11.1	Lipohypertrophy	-	-	+	-	-	-

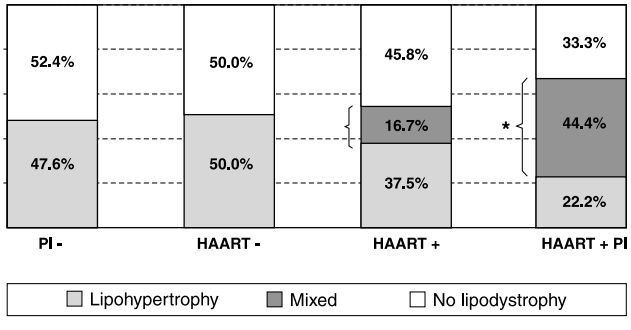
DIAG = age at diagnosis (months); EPM = energy-protein malnutrition; F = female; IR = insulin resistance; M = male; SS = short stature; TG = triglycerides; TOR = time on regimen in use at study outset (in months).
Nucleoside analog reverse transcriptase inhibitors: 3TC = lamivudine ; ABC = abacavir; AZT = zidovudine; d4T = stavudine; ddI = didanosine.
Non-nucleoside reverse transcriptase inhibitors: EFZ = efavirenz; NVP = nevirapine.
Protease inhibitors: IDV = indinavir; LPV/r = lopinavir + ritonavir; NFV = nelfinavir; RTV = ritonavir.

were observed in 20, 13.3 and 43.3% of the children with AIDS, respectively.

Clinical lipodystrophy was observed in 16 (53.3%) of the children with AIDS. Four children (13.3%) exhibited mixed lipodystrophy, and 12 (40.0%) had lipohypertrophy.

Children who were on HAART regimens with protease inhibitors exhibited a greater percentage of mixed lipodystrophy, with the difference between them and the other groups being statistically significant (44.4 vs. 16.7%; p = 0.004) (Figure 1).

There were no statistically significant differences observed in terms of presence of lipodystrophy among the children and adolescents related to sex, age > 10 years, presence of dyslipidemia(s) (LDL-c, HDL-c and triglycerides) or insulin resistance (Table 3).



PI = protease inhibitors; HAART = highly active antiretroviral therapy.
All of the children taking PI were also on HAART.
* Significance level according to the chi-square test: HAART + PI with mixed lipodystrophy = 44.4 vs. 16.7%; p = 0.004.

Figure 1 - Presence or absence of lipodystrophy in the study population, by medication regimen

Table 3 - Abnormal test results for the variables studied for the groups of children with acquired immunodeficiency syndrome with and without clinical lipodystrophy

Variable	Lipodystrophy present (n = 16) n (%)	Lipodystrophy absent (n = 14) n (%)	p*
Male sex	7 (43.7)	7 (50)	0.509
Age > 10 years	8 (50.0)	4 (28.6)	0.176
LDL-cholesterol abnormal	3 (18.7)	3 (21.4)	0.605
HDL-cholesterol abnormal	2 (12.5)	2 (14.3)	0.648
Triglycerides abnormal	4 (25)	3 (21.4)	0.581
HOMA-IR > 3	0 (0)	1 (7.1)	0.467

HOMA-IR = homeostasis model assessment.
* Significance level according to chi-square test or Fisher's exact test.

Discussion

In this study we found dyslipidemia in 60% of a group of children and adolescents infected with HIV. The prevalence of hypertriglyceridemia found in our study (43.3%) was greater than observed in a pediatric cohort study carried out in Houston (28%), but lower than the prevalence observed in a Mexican study (79.2%).[21,22]

In individuals infected by HIV, dyslipidemia is the result of the combination of infection by the virus, the effect of antiretroviral drugs and genetic factors. The HIV infection itself is associated with a proatherogenic lipid profile characterized by increased triglycerides and a concentration of the lower density particles of the LDL fraction of cholesterol and a reduction in HDL C levels.[23,24]

When compared with indinavir, nelfinavir and atazanavir, ritonavir is the protease inhibitor most associated with lipid profile abnormalities.[25] With relation to non-nucleoside reverse transcriptase, studies suggest that using nevirapine leads to fewer lipid profile abnormalities than efavirenz. Among the nucleoside analog reverse transcriptase inhibitors, more lipid profile abnormalities have been observed in association with d4T than with tenofovir and abacavir.[23]

A recent cohort study found that, after adjusted multifactorial analysis, there was a relationship between the use of protease inhibitors, the development of lipodystrophy and acute myocardial infarction in adults.[26]

Human immunodeficiency virus infections can result in chronic oxidative stress with apoptosis of T-lymphocytes and increases in viral replication rates due to activation of nuclear factor kappa B. Furthermore, mitochondrial toxicity, which is an adverse event observed with antiretroviral drugs, can contribute to exacerbation of oxidative stress. This toxicity may be responsible for the lipodystrophy that is associated with the use of highly active antiretroviral therapy (HAART). Adult patients starting HAART regimens frequently develop increased central adiposity and a reduction in lean mass during the first 24 weeks of treatment and may develop insulin resistance, dyslipidemia and peripheral lipoatrophy after 6 months on the treatment.[27,28]

In this study, we observed that children with AIDS who were on HAART with protease inhibitors exhibited a greater frequency of clinical lipodystrophy than those on regimens without protease inhibitors and than controls. Although the mechanisms by which protease inhibitors lead to lipodystrophy syndrome have not been entirely elucidated, some hypotheses have been proposed: mitochondrial damage; compromised pre-adipocyte differentiation, leading to adipocyte apoptosis in certain regions; reductions in transcription factors related to adipogenesis; increased expression and secretion of the proinflammatory cytokines (tumor necrosis factor α and interleukin 6) involved in modifying adipocyte function and reducing adiponectin; increases in leptinemia associated with the accumulation of central fat and insulin resistance; and increased levels of visfatin and retinol binding protein 4.[6,29]

We did not observe a relationship between clinical lipodystrophy and lipid and glucose metabolism abnormalities in these children and adolescents with AIDS. In order to explain this finding, we developed some hypotheses: the low age of the study population; limitations due to the study methodology (cross-sectional), which did not allow for evaluation of the development of the parameters studied over time; and limitations of the clinical examination method used to assess body fat redistribution, without supplementary tests such as DXA.[9]

The importance of early identification of lipodystrophy syndrome lies in the fact that it is related to future development of cardiovascular events.[26,30] The redistribution of body fat may also prejudice compliance with treatment, causing depression and low self-esteem, especially among

adolescents. Few studies have dealt with prevention and treatment of redistribution of body fat and lipodystrophy syndrome in the pediatric age group.[9]

Bearing in mind the high frequency of dyslipidemia and lipodystrophy found in this study population, indicating a relationship with the antiretroviral regimen employed, it is pertinent to emphasize the importance of multidisciplinary care for children and adolescents with AIDS, including wide-ranging nutritional education and lifestyle changes, in order to minimize the risk of the development of future complications, such as cardiovascular diseases.

References

1. Centers for Disease Control and Prevention. Guidelines for the use of antiretroviral agents in pediatric HIV infection. http://www.aidsinfo.nih.gov Access: 10/10/2008.
2. Jaquet D, Lèvine M, Ortega-Rodriguez E, Faye A, Polak M, Vilmer E, et al. Clinical and metabolic presentation of the lipodystrophic syndrome in HIV-infected children. AIDS. 2000;14:2123-8.
3. Romanelli RM, Pinto JA, Melo LJ, Vasconcelos MA, Pereira Rde M. Effectiveness of dual and triple antiretroviral therapy in the treatment of HIV-infected children. J Pediatr (Rio J). 2006;82:260-5.
4. Noor MA, Seneviratne T, Aweeka FT, Lo JC, Schwarz JM, Mulligan K, et al. Indinavir acutely inhibits insulin-stimulated glucose disposal in humans: a randomized placebo controlled study. AIDS. 2000;16:F1-8.
5. Barbaro G, Fisher SD, Lipshultz SE. Pathogenesis of HIV associated cardiovascular complications. Lancet Infect Dis. 2001;1:115-24.
6. Pinti M, Salomoni P, Cossarizza A. Anti-HIV drugs and the mitochondria. Biochem Biophys Acta. 2006;1757:700-7.
7. Tang AM, Lanzilotti J, Hendricks K, Gerrior J, Ghosh M, Woods M, et al. Micronutrients: current issues for HIV care providers. AIDS. 2005;19:847-61.
8. Mc Crindle BW, Urbina EM, Dennison BA, Jacobson MS, Steinberger J, Rocchini AP, et al. Drug therapy of high-risk lipid abnormalities in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young, with the Council on Cardiovascular Nursing. Circulation. 2007;115:1948-67.
9. Alves C, Oliveira AC, Brites C. Lipodystrophic syndrome in children and adolescents infected with the human immunodeficiency virus. Bras J Infect Dis. 2008;12:342-8.
10. Centers for Disease Control and Prevention. 1994 Revised classification system for human immunodeficiency virus infection less than 13 years age. MMWR. 1994;43:1-10.
11. Associação Brasileira de Empresas de Pesquisa - 2003. http://www.abep.org/codigosguias/Criterio_Brasil_2008.pdf. Access: 07/07/2009.
12. Monteiro CA, Nazario CL. Evolução de condicionantes ambientais da saúde na infância na cidade de São Paulo (1984-1996). Rev Saude Publica. 2000;34:13-8.
13. World Health Organization: Physical Status. The use and interpretation of anthropometry. WHO Technical Report Series 854. Geneva: WHO; 1995.
14. Kuczmarski RJ, Ogden CL, Grummer-Strawn. CDC growth charts: United States. Advance data from vital and health statistics; nº. 314. Hyattsville, MD: NCHS; 2000.
15. Marshall WA, Tanner JM. Growth and physiological development during adolescence. Annu Rev Med. 1975;19:283-300.
16. Valente AM, Reis AF, Machado DM, Succi RC, Chacra R. Alterações metabólicas da síndrome lipodistrófica do HIV. Arq Bras Endocrinol Metab. 2005;49:871-81.
17. National Cholesterol Education Program (NCEP): highlights of the report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics. 1992;89:495-501.
18. Tresaco B, Bueno G, Pineda I, Moreno LA, Garagorri JM, Bueno M. Homeostatic model assessment (HOMA-IR) index cut-off values to identify the metabolic syndrome in children. J Physiol Biochem. 2005; 61:381-8.
19. SPSS. SPSS Base 13.0: Base Users Guide. Chicago, 2004.
20. Dean AG. Epi Info™ and Epi Map: Current status and plans for Epi Info™ 2000. J Pub Health Manag Pract. 1999;5:54-7.
21. Amaya RA, Kozinetz CA, McMeans A, Schwarzwald H, Kline MW. Lipodistrophy syndrome in human immunodeficiency virus-infected children. Pediatr Infect Dis J. 2002;21:405-10.
22. Santos FS, Rangel LG, Saucedo GP, Rosales GV, Novales MG. Hypertriglyceridemia and hypercholesterolemia in human immunodeficiency vírus-1 infected children treated with protease inhibitors. Arch Med Res. 2006;37:129-32.
23. Brett-Major DM, Ganesan A. Dyslipidemia management in patients with human immunodeficiency vírus. Infect Dis Clin Pract. 2007;15:7-16.
24. Carr A, Samaras K, Thorisdottir A. Diagnosis, pediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. Lancet. 1999;353:2093-9.
25. Young J, Weber R, Rickenbach M, Furrer H, Bernasconi E, Hirschel B, et al. Lipid profiles for antiretroviral-naive patients starting PI- and NNRTI-based therapy in the Swiss HIV cohort study. Antivir Ther. 2005;10:585-91.
26. DAD Study Group, Friis-Møller N, Reiss P, Sabin CA, Weber R, Monforte A, et al. Class of antiretroviral drugs and the risk of myocardial infarction. DAD Study Group. N Engl J Med. 2007;356:1723-35
27. Carr A, Miller J, Law M, Cooper DA. A syndrome of lipoatrophy, lactic acidemia and liver dysfunction associated with HIVnucleoside analogue therapy: contribution to protease inhibitor-related lipodystrophy syndrome. AIDS. 2000;14:F25-32.
28. Mallon PW, Miller J, Cooper DA, Carr A. Prospective evaluation of the effects of antiretroviral therapy on body composition in HIV-1 infected men starting therapy. AIDS. 2003;17:971-9.
29. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa nacional de DST e AIDS. Guia de tratamento clínico da infecção pelo HIV em crianças. Secretaria de Vigilância em Saúde. Programa Nacional de DST e AIDS. 3ª ed. Brasília: Ministério da Saúde; 2006.
30. May M, Sterne JA, Sabin C, Costagliola D, Justice AC, Thiébaut R, et al; Antiretroviral Therapy (ART) Cohort Collaboration. Prognosis of HIV-1-infected patients up to 5 years after initiation of HAART: collaborative analysis of prospective studies. AIDS. 2007;21:1185-97.

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