Cardiovascular abnormalities and carotid intima-media thickness (cIMT) among HIV-infected adolescents receiving long-term highly antiretroviral therapy in Thailand: A cross-sectional study with HIV-uninfected healthy controls

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Introduction

Cardiovascular diseases are commonly found in HIV-infected patients with advanced HIV disease. Before the era of HAART, 26% of HIV-infected children were found to have decreased cardiac contractility.1 Among the cardiovascular abnormalities were asymptomatic, with potential for progression.2 A few studies found HIV-infected children had increased carotid intima-media thickness (cIMT) compared to normal children.3 The increased cIMT is a marker of cardiovascular disease risk in adult populations.4 Antiretroviral therapy was found to improve cIMT after 48 weeks of HAART.5

Objective

This study aimed to evaluate the cardiovascular abnormalities and cIMT in perinatal HIV-infected adolescents in Thailand.

Indication criteria

• Perinatal HIV-infected adolescents or healthy adolescents
• Age between 12-15 years old
• No clinical signs or symptoms of cardiovascular disease
• Normal chest X-ray taken within the past 3 months
• Receiving HAART for at least 6 months in HIV-infected subjects

Exclusion criteria

• Presence of congenital heart disease or any known cardiovascular disease or condition
• Having active opportunistic infection except for tuberculosis that have been receiving treatment for more than 1 month
• History of taking drugs that may affect cardiac function
• Pregnancy

Materials and methods

A cross-sectional study with single visit was conducted in HIV-infected adolescents and Healthy controls at the Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, from July 2012 to January 2013.

• The study procedure included:
  1. Physical examination with heart rate, blood pressure measurement, weight and height measurement,
  2. Chest X-ray to assess cardiothoracic ratio, lung infections, osteopenia in adolescents.
  3. Laboratory tests for CBC, ESR, CRP, HIV load, CD4 count.
  4. HIV-infected adolescents were also tested for CD20, HIV-1 RNA.

Echocardiography, was to assess cardiac anatomy and functions

All study participants were undergo a protocol directed transthoracic echocardiography (2 Dimensional, M mode and Doppler evaluation) using a Philips E 33 model echocardiography machine and a transducer frequency of 5 MHz, or higher.

The procedure was performed by experienced pediatric cardiologist who blind for subject’s HIV status.

The echocardiographic parameters measured: systolic function, diastolic function, global cardiac function, pulmonary systolic function, pericardial effusion, LV hypertrophy

ECEF = Left ventricular ejection fraction; P AP = Pulmonary artery pressure; LVIMP = Left ventricular index of myocardial performance

- The control ECEF will be the same by cardiologist (right after echocardiography, using the US’s device (General Electric; USA) equipped with a 10 mmHg linear probe
- cIMT was calculated from the mean of 2 measurements at each site (right and left side). For proximal CCA (0.39 mm), distal CCA, and ICA measured the far and near wall for 2 times each, resulting in a total of 24 measurements per subject.

Results

Enrolled: 100 HIV-infected, 50 healthy controls

All HIV-infected adolescents had perinatal infection and 32% experienced OCC clinical stage C

At the entry of study, the median CD4 count was 504 (24-2,121) cell/mm^3

70% had CD4 ≥ 500 cell/mm^3 and 82% had HIV RNA < 40 copies/ml

The median duration of ART was 123.3 (6-180) months

49% were receiving protease inhibition (PI)

The median duration of PI therapy was 63.9 (6.5-133.5) months

HIV-infected adolescents had a higher triglyceride and lower HDL than healthy controls

HIV-infected adolescents had a higher median LV RMP than healthy controls suggesting poorer myocardial performance.

There were 4 HIV-infected adolescents, and none healthy control, have abnormal myocardial performance; three with ECEF < 55% and one with ECEF ≥ 55%

No difference of cIMT between HIV-infected adolescents and healthy controls

HIV-infected adolescents who receiving PI treatment > 6 months was associated with higher median cIMT of proximal CCA (0.39 ± 0.37 mm, P=0.01) and distal CCA (0.33 ± 0.36 mm, P=0.04)

Literature cited


Table 1. Demographics and clinical characteristics of HIV-infected adolescents and healthy controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV-infected (N=100)</th>
<th>Healthy controls (N=50)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>15.0 (12.2-20.1)</td>
<td>16.15 (15.3-20.9)</td>
<td>0.20</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>50 (50)</td>
<td>49 (49)</td>
<td>0.89</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>43.8 (27.7-57.3)</td>
<td>50.15 (38.6-51.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155 (139-167)</td>
<td>165.2 (146.9-176.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m^2)</td>
<td>18.1 (12.3-20.4)</td>
<td>18.4 (16.8-20.2)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Table 2. Lipid profile and hs-CRP in HIV-infected adolescents and healthy controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=100</th>
<th>N=50</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>177 (130-197)</td>
<td>172 (130-196)</td>
<td>0.68</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>173 (95-345)</td>
<td>62 (27-230)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>120.0 (60.1-234.9)</td>
<td>120.6 (62.7-177.6)</td>
<td>0.34</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>50 (39-99)</td>
<td>57 (37-129)</td>
<td>0.007</td>
</tr>
<tr>
<td>Non-HDL cholesterol, n (%)</td>
<td>25 (25.0)</td>
<td>12 (24.0)</td>
<td>0.867</td>
</tr>
<tr>
<td>Hypertriglyceridemia, n (%)</td>
<td>23 (23.0)</td>
<td>12 (24.0)</td>
<td>0.867</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>16 (16.0)</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Hyper HDL cholesterol, n (%)</td>
<td>16 (16.0)</td>
<td>8 (8.0)</td>
<td>0.037</td>
</tr>
<tr>
<td>Hypo HDL cholesterol, n (%)</td>
<td>16 (16.0)</td>
<td>7 (7.0)</td>
<td>0.037</td>
</tr>
</tbody>
</table>

Table 3. The echocardiographic measurements of cardiac function and carotid IMT in HIV-infected adolescents and healthy controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV-infected (N=100)</th>
<th>Healthy controls (N=50)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (±SD)</td>
<td>64 (±30.6)</td>
<td>65 (±30.8)</td>
<td>0.829</td>
</tr>
<tr>
<td>Mean PAP (mmHg)</td>
<td>19 (±10)</td>
<td>19 (±12)</td>
<td>0.38</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>2.0 (±3.0)</td>
<td>2.0 (±3.0)</td>
<td>0.004</td>
</tr>
<tr>
<td>Proximal CCA IMT (mm)</td>
<td>0.38 (±0.34-0.475)</td>
<td>0.375 (±0.308-0.452)</td>
<td>0.398</td>
</tr>
<tr>
<td>Distal CCA IMT (mm)</td>
<td>0.3882 (±0.2725-0.475)</td>
<td>0.38 (±0.3225-0.48)</td>
<td>0.541</td>
</tr>
<tr>
<td>Internal carotid IMT (mm)</td>
<td>0.3550 (±0.23-0.5137)</td>
<td>0.355 (±0.321-0.645)</td>
<td>0.464</td>
</tr>
<tr>
<td>Overall cIMT (mm)</td>
<td>0.373 (±0.284-0.451)</td>
<td>0.37 (±0.324-0.486)</td>
<td>0.744</td>
</tr>
</tbody>
</table>

Conclusions

- HIV-infected adolescents had relatively normal myocardial function and very similar cIMT as healthy adolescents
- However, increased cIMT was found in HIV-infected adolescents receiving PI regimen
- Receiving PI was associated with hypertriglyceridemia and increased cIMT
- HIV-infected adolescents had higher triglyceride level and lower HDL
- Our study support that HIV patients who receiving PI therapy should be screened for hypertriglyceridemia and may be candidate for lip-lowering therapies that can improve endothelial function which may prevent aderent cardiovascular events
- Longer-term follow up is needed to evaluate the CVD risk in this population

Acknowledgements

We would like to thank all our patients, the TREAT Asia/HIV-Asia Network, the Thailand National Children’s Research Foundation for AIDS Research, Thailand, the Office of academician; The Foundation for AIDS Research, Bangkok, Thailand, Kulkanya Chokephaibulkit MD, MA for editorial assistance, for critical reading, and suggestions on the manuscript. The study was supported by the Thailand National Children’s Research Foundation for AIDS Research, Thailand.

* P-values were calculated in both per-protocol analysis and as intention to treat analysis or waveform analysis

Presented at IAS 2013 – Kuala Lumpur, Malaysia