Prevalence of Metabolic Associated Cardiovascular Risk Factor Abnormalities in Human Immunodeficiency Virus Treated Patients

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Abstract

Background: The prevalence of metabolic abnormalities and associated cardiovascular risk in HIV-infected adults on combination antiretroviral therapy is unknown in Siriraj hospital. This analysis was 1) to find the prevalence of metabolic associated cardiovascular risk factor abnormalities in HIV-infected patients 2) to determine the time to the development of metabolic abnormalities and associated cardiovascular risk and 3) to find predictive factors for the development of drug-related metabolic abnormalities.

Methods: In this retrospective cohort study, data were collected from the medical record form in HIV treated patients who received combination antiretroviral therapy and follow up blood chemistries during treatment until November 2007. The prevalence and time duration to the development of metabolic associated cardiovascular risk factor abnormalities were calculated using the survival-analysis technique and finding predictive factors by the Cox Regression analysis technique.

Results: 86 of 180 patients had metabolic associated cardiovascular risk abnormalities. The prevalence was 47.8 % (95% confidence interval, 40.6 to 55). The time to the development of metabolic abnormalities after treatment by combination antiretroviral therapy was 791 ± 486 days. The predictive factors were as follows: 1) baseline serum cholesterol level ≥ 160 mg/dl, Hazard ratio 1.90 (95 % confidence interval, 1.22 to 2.97); p 0.004, 2) baseline serum triglyceride level ≥ 120 mg/dl Hazard ratio 2.05 (95 % confidence interval, 1.32-3.18); p 0.002 and 3) male gender Hazard ratio 2.01 (95 % confidence interval 1.3 to 3.2); p 0.003. The prevalence of combination antiretroviral therapy associated metabolic abnormalities between protease inhibitor and Non-nucleoside reverse-transcriptase inhibitors were not different.

Conclusions: Combination antiretroviral therapy was independently associated with the prevalence (47.8 %) to develop metabolic associated cardiovascular risk factor abnormalities. The duration of treatment to development was 791 ± 486 days. The predictive factors for the development of metabolic abnormalities were baseline serum cholesterol level ≥ 160 mg/dl, baseline serum triglyceride level ≥ 120 mg/dl and male gender. Metabolic associated cardiovascular risk factor abnormalities could be detected with all combination antiretroviral therapies. The physician should be aware of early detection of metabolic abnormalities in all HIV treated patients.

Keywords: HIV infected patient, Combination antiretroviral therapy, Metabolic, Cardiovascular risk factor

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Introduction

The benefit of combination antiretroviral therapy has changed the natural history of Human immunodeficiency virus (HIV) infected patients, and has led to a significant reduction in morbidity and mortality. However, use of antiretroviral therapy is known to be associated with changes in metabolic abnormalities, including dyslipidemia, insulin resistance and overt diabetes mellitus (1-2, 3). These are well-known risk factors for cardiovascular disease (4). The prevalence of metabolic abnormalities and cardiovascular risk in HIV-infected adults on combination antiretroviral therapy is unknown in Siriraj hospital. The primary objective of this analysis was to find the prevalence...
of metabolic associated cardiovascular risk factor abnormalities in HIV-infected adults on combination antiretroviral therapy in Siriraj hospital. A secondary objective was to determine the time to development of metabolic associated cardiovascular risk abnormalities in HIV-treated patients and predictive factors for the development of drug-related metabolic abnormalities.

Methods

Design

A retrospective-cohort study design was used to determine the development of metabolic associated cardiovascular risk factor abnormalities in HIV treated patients in Siriraj hospital. This study was approved by the Ethics committee of Siriraj Hospital.

Collection of data

We reviewed the medical records from the HIV-outpatient infectious unit in Siriraj hospital. The data was recorded by the same investigator who reviewed the medical records. The sample populations were HIV-infected adults who met the following criteria: 1) HIV-infected patients managed by combination antiretroviral therapy at the outpatient Infectious Unit in Siriraj hospital. 2) Age > 18 years old. 3) Had baseline lab and at least one lab after treatment with antiretroviral therapy. Patients were excluded from the study if 1) withdrawal of combination antiretroviral therapy. 2) active opportunistic infection. 3) known history of dyslipidemia, diabetes mellitus, or Impaired fasting glucose.

The definitions of metabolic abnormalities were defined from the National cholesterol education program (NCEP) (5) and included the following: hypercholesterolemia (serum total cholesterol > 200 mg/dl), hypertriglyceridemia (serum triglyceride or TG > 200 mg/dl), combined hyperlipidemia (Cholesterol and TG > 200 mg/dl), hypoalphalipoproteinemia (HDL-C < 40 mg/dl), normal fasting glucose: (Fasting plasma glucose < 110 mg/dl), impaired fasting plasma glucose (FPG ≥ 110 and <126 mg/dl), and a provisional diagnosis of diabetes (FPG ≥ 126 mg/dl).

Statistical analysis

The baseline demographic data is presented as descriptive statistics (Table 1) using the mean and standard deviation for continuous data and percentage in categorical data. The prevalence of metabolic abnormalities and cardiovascular risk factors was presented by percentage with a 95% confidence interval. The time to develop metabolic associated cardiovascular risk abnormalities in HIV-infected adults on antiretroviral therapy is presented by Survival analysis. Predictive factors for the development of metabolic abnormalities was analysed by Cox regression analysis.

Results

One hundred and eighty patients were enrolled in this study. The patients included one hundred males and eighty females. Eighty-six patients developed metabolic associated cardiovascular risk abnormalities.

The prevalence of metabolic abnormalities in HIV-treated patients was 47.8% (95% confidence interval, 40.6 to 55). The time to development of metabolic abnormalities after treatment by combination antiretroviral therapy was 791 ± 486 days (Figure 1). The male gender developed metabolic abnormalities more rapidly than females (Figure 2) p 0.003, Hazard ratio 2.0 (95% confidence interval 1.3 to 3.2). The predictive factors for the development of metabolic abnormalities were 1) baseline serum cholesterol level ≥ 160 mg/dl (Figure 3), Hazard ratio 1.90 (95% confidence interval 1.3 to 3.2).

Figure 1. Survival curve of HIV-treated patients with metabolic abnormalities during follow up
Prevalence of Metabolic Associated Cardiovascular Risk Factor Abnormalities in Human Immunodeficiency Virus Treated Patients.

Table 1. Demographic and HIV infection characteristics of 180 patients

<table>
<thead>
<tr>
<th></th>
<th>Total (n=180)</th>
<th>Event (n=86)</th>
<th>No event (n=94)</th>
<th>p value</th>
<th>HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (days)</td>
<td>759 ± 497</td>
<td>791 ± 486</td>
<td>731 ± 508</td>
<td>0.42</td>
<td>2.0 (1.3-3.2)</td>
</tr>
<tr>
<td>Male</td>
<td>100</td>
<td>59 (68.6)</td>
<td>41 (43.6)</td>
<td>0.003</td>
<td>1.6 (1.3-1.9)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>36.9 ± 10.3</td>
<td>38.8 ± 10.5</td>
<td>35.3 ± 9.9</td>
<td>0.16</td>
<td>2.0 (1.3-3.2)</td>
</tr>
<tr>
<td>Regimen:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTI+NNRTI</td>
<td>168</td>
<td>79 (91.9)</td>
<td>89 (94.7)</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>NRTI+NNRTI+PI</td>
<td>12</td>
<td>7 (8.1)</td>
<td>5 (5.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol level (mg/dl)</td>
<td>159 (46,194)</td>
<td>168 (98,193)</td>
<td>149 (46,194)</td>
<td>0.03</td>
<td>2.0 (1.3,3.1)</td>
</tr>
<tr>
<td>Total cholesterol ≥160 mg/dl</td>
<td>87</td>
<td>55 (64)</td>
<td>32 (34)</td>
<td>0.002</td>
<td>2.0 (1.3,3.1)</td>
</tr>
<tr>
<td>LDL cholesterol level (mg/dl)</td>
<td>91 (15,145)</td>
<td>98 (15,173)</td>
<td>88 (15,4,129)</td>
<td>0.20</td>
<td>1.3 (1.0,1.6)</td>
</tr>
<tr>
<td>HDL cholesterol level (mg/dl)</td>
<td>39 (11,75)</td>
<td>37.8 (11,8,75)</td>
<td>40 (20,75)</td>
<td>0.64</td>
<td>1.4 (1.0,2.0)</td>
</tr>
<tr>
<td>Triglyceride level (mg/dl)</td>
<td>117 (44,295)</td>
<td>133 (50,295)</td>
<td>108 (44,197)</td>
<td>&lt;0.001</td>
<td>1.6 (1.1,2.4)</td>
</tr>
<tr>
<td>≥120 mg/dl</td>
<td>89</td>
<td>53 (61.6)</td>
<td>36 (38.3)</td>
<td>&lt;0.001</td>
<td>1.6 (1.1,2.4)</td>
</tr>
<tr>
<td>Fasting blood sugar level (mg/dl)</td>
<td>90 (60,121)</td>
<td>92 (60,121)</td>
<td>89 (67,115)</td>
<td>0.17</td>
<td>1.2 (0.9,1.6)</td>
</tr>
<tr>
<td>CD4 cell count (x106 cell/l)</td>
<td>95 (2,514)</td>
<td>89 (2,496)</td>
<td>99 (2,514)</td>
<td>0.23</td>
<td>1.2 (0.9,1.6)</td>
</tr>
</tbody>
</table>

Event: serum total cholesterol ≥ 200 mg/dl, or Fasting plasma glucose ≥ 126 mg/dl
All data were expected: Mean ± SD, median (min, max), n (%) P: p-value (Cox Regression Analysis)
NRTI = Nucleoside analogues reverse transcriptase inhibitors
NNRTI = Nonnucleoside reverse transcriptase inhibitors
PI = Protease inhibitors

Discussion

This study shows the prevalence of metabolic abnormalities to be 47.8% in HIV-treated patients. The time duration to develop the metabolic associated cardiovascular risk factor abnormalities were within 2-3 years. The most common metabolic abnormality was hypercholesterolemia and the male gender developed it more rapidly than the female gender. The mechanism could be explained by the fact that antiretroviral therapy may lead to an altered flux of substrates, including free fatty acids, as well as the accumulation of intramyocellular lipid, alteration in adipokine levels (e.g., a low level of adiponectin), and a reduction in PPAR-gamma expression in subcutaneous adipocytes. Moreover, antiretroviral therapy may also contribute to an altered glucose homeostasis (3, 6-8). A previous study (9) reported the association of protease inhibitor exposure with metabolic abnormalities.

In our study, we found the predictive factors for the development of metabolic abnormalities were as follows: 1) baseline serum cholesterol level ≥ 160 mg/dl, 2) baseline serum triglyceride level ≥ 120 mg/dl, and 3) male gender.

Combination antiretroviral therapy substantially improves the prognosis of HIV-infected patients at risk...
for acquired immunodeficiency syndrome (AIDS). The substantial benefits of combination antiretroviral therapy clearly continue to outweigh the increased cardiovascular risk associated with therapy. Nevertheless, it is less expensive to educate all HIV treated patients for primary cardiovascular disease prevention, to follow a diet control program and to do regular exercise to promote their general health (10-11). Moreover smoking cessation can save some money that can be used to purchase combination antiretroviral drugs. Physicians should be aware of early detection of metabolic abnormalities in all HIV treated patients.

Several limitations in this study design should be noted. This study was not a randomized control trial and thus we could not distribute confounding factors that effect outcome. Furthermore, some medical records were incomplete; we lost some data especially blood sugars because the physician tended to check lipid profiles more. This could explain why this study showed a prevalence for dyslipidemia more than impaired fasting blood sugar.
References


การศึกษาหาความสูงของความมีค่าปกติทางความดันโลหิตในส่วนที่เกี่ยวข้องกับปัจจัยเสี่ยงของการเป็นโรคหัวใจและหลอดเลือดในผู้ป่วยเด็กช่วงโซ่อิโวที่ได้รับการรักษาด้วยยาต้านไวรัส

สาขาวิทยาการ ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล

บทก㎏ย์

วัตถุประสงค์: ความสูงของความมีค่าปกติทางความดันโลหิตในส่วนที่เกี่ยวข้องกับปัจจัยเสี่ยงของโรคหลอดเลือดหัวใจและหลอดเลือดที่เกิดขึ้นจากการที่ผู้ป่วยเด็กช่วงโซ่อิโวที่ได้รับการรักษาด้วยยาต้านไวรัส จึงเป็นที่น่าสนใจในการศึกษา

วิธีการศึกษา: ใช้วิธีการศึกษาฟีดแบ็คจากผู้ป่วยที่ได้รับการรักษาด้วยยาต้านไวรัส

ผลของการศึกษา: ผู้ป่วย 86 รายจาก 180 ราย พบว่ามีความมีค่าปกติทางความดันโลหิตที่เกี่ยวข้องกับปัจจัยเสี่ยง คือการเป็นโรคหัวใจและหลอดเลือด คิดเป็นข้อที่สูง ร้อยละ 47.8% (95% confidence interval 40.6-55) โดยที่ ระยะเวลาของการเกิดความมีค่าปกติทางความดันโลหิตที่เกี่ยวข้องกับปัจจัยเสี่ยงในผู้ป่วย คือ 791 ± 481 วัน และปัจจัยที่ทำให้ผู้ป่วยมีโอกาสเกิดการเกิดความมีค่าปกติทางความดันโลหิตคือ 1) โรคหลอดเลือดหัวใจ 2) โรคหลอดเลือดที่เกี่ยวข้องกับปัจจัยเสี่ยงที่เป็นโรคหัวใจและหลอดเลือด 3) โรคหลอดเลือดที่เกี่ยวข้องกับปัจจัยเสี่ยงที่เป็นโรคหัวใจและหลอดเลือดอื่นๆ ที่พบจากการศึกษาตัวอย่างจากวิสัยทัศน์

สรุปผลการศึกษา: อาการคัด้านไวรัสนำเข้าผู้ป่วยที่ได้รับการรักษาด้วยยาต้านไวรัสต้องดูดความมีค่าปกติทางความดันโลหิตที่เกี่ยวข้องกับปัจจัยเสี่ยงที่เกี่ยวข้องกับการเป็นโรคหัวใจและหลอดเลือดในผู้ป่วยเด็กช่วงโซ่อิโว ซึ่งแพทย์ผู้ดูแลควรรักษาความระคายเคืองและให้ระวังอาการผิดปกติเกิดขึ้น

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