Effect of Aerobic Exercise Training in Older HIV-Infected Patients

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3rd International HIV & Aging Conference
November 5, 2012

University of Maryland Baltimore Claude D. Pepper Older Americans Independence Center
Baltimore VA Geriatric Research, Education and Clinical Center (GRECC)
HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity

Steven G Deeks, Andrew N Phillips

Box 2 Non-AIDS related complications that may be more common in patients with HIV

- Hypertension
- Diabetes mellitus and insulin resistance
- Cardiovascular disease
- Pulmonary hypertension
- Cancer
- Osteopenia and osteoporosis
- Liver failure
- Kidney failure
- Peripheral neuropathy
- Frailty
- Cognitive decline and dementia
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Exercise is effective prevention & treatment

- Cardiorespiratory fitness
- Muscle strength & quality
- Cardiac function
- Capillary density
Cardiorespiratory Fitness is Reduced 40% in HIV-infected vs. Healthy Adults

Oursler, AIDS Research HR, 2006
Muscle mass is lower in HIV+ men compared to healthy controls, but 5-year decline similar

Background: Exercise in Older Adults

• Aerobic exercise (AEX) and resistive training (RT)
  – Can be used alone or in combination, based on goal
  – Vary by intensity, duration, and type of equipment

• Aerobic exercise in younger HIV-infected adults
  – ↑ 12-25% VO2peak (Stringer, 1998; Perna, 1999; Terry, 2006)
  – ↓ Levels of IL-6, TNF-α, hsCRP (Lindegaard, 2008)

• Resistive training in older (62+yr) HIV-infected adults
  – Free weights 2x week for 1 year (de Souza, 2008)
  – Strength increased 74-122% (p < 0.02)
  – Improved chair stand and short distance walk
The combination of HIV, aging, and cardiovascular disease potentiates the loss of cardiorespiratory fitness and strength, resulting in decreased physical function.
To determine the effect of AEX in older HIV + men on:
- Cardiorespiratory Fitness
- Ambulatory function
- Biomarkers of chronic inflammation
Aerobic Exercise Intervention

- **Design:**
  - Randomized to low-intensity or high-intensity aerobic training (AEX)
  - 3x week for 16 weeks
  - Supervised and center-based
  - Encouraged to maintain calorie intake (no △ diet)
  - Baseline & 16 week testing included plasma for biomarkers of chronic inflammation

- **Low-intensity AEX:** 1 mile self-paced walking on indoor track

- **High-intensity AEX:** treadmill training with target of 45-60 minutes  @ 70-80% HRR (heart rate reserve = (HRmax – HRrest) + HR rest)
**Inclusion Criteria:**
- Age 50+ years
- Sedentary
- Community-dwelling
- No AIDS illness 6+ months
- HAART 6+ months

**Exclusion Criteria**
- Poorly controlled HTN (SBP/DBP>180/105)
- CHF (class III or IV)
- Anemia (hgb< 10gm/dl)
- End stage liver or kidney disease
- B-Blocker medication
Chart Review
N = 74

Screening H&P
N = 38

Baseline testing
N = 31

Randomized
N = 22

36 Excluded:
age<50, hgb<10
no HIV meds,
+ B-blocker

7 Excluded:
active CVD,
CA, or AIDS

6 Excluded:
anemia, CA
ischemia
3 Incomplete

Low- Intensity AEX
N = 11
1 knee pain (OA)
1 stroke
2 LTFU
7 Subjects

High- Intensity AEX
N = 11
1 knee pain (OA)
1 LTFU
9 Subjects
<table>
<thead>
<tr>
<th>Variable</th>
<th>Lo-AEX n= 7</th>
<th>Hi-AEX n= 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 (1)</td>
<td>57 (2)</td>
</tr>
<tr>
<td>CD4 Count (cells/mm$^3$)</td>
<td>469 (94)</td>
<td>481 (66)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>97(3)</td>
<td>77(5)</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>34 (1)</td>
<td>22 (2)</td>
</tr>
<tr>
<td>VAT (cm$^2$)</td>
<td>190(80)</td>
<td>108(69)</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>133 (23)</td>
<td>113 (12)</td>
</tr>
<tr>
<td>Insulin (pmol/l)</td>
<td>154 (17)</td>
<td>67 (13)</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>80 (11)</td>
<td>87 (13)</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>221 (84)</td>
<td>117 (14)</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>40 (2)</td>
<td>47 (6)</td>
</tr>
</tbody>
</table>
Baseline hsCRP Inversely Correlated with Hemoglobin and VO2peak

$r = -0.71$

$p < 0.01$

$r = -0.41$

$p = ns$
High-AEX Increases VO2peak

VO2peak, L/min

Baseline 16-week

Low-AEX

High-AEX

+ 17%

p=0.02

p= ns
High-AEX and Low-AEX
Increase Ambulatory Function

Low-AEX
+ 11%
\( p = 0.01 \)

High-AEX
+ 12%
\( p = 0.01 \)
## AEX Did Not Significantly Reduce CVD Risk Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Change 16 wks - baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lo-AEX n= 7</td>
</tr>
<tr>
<td>Weight</td>
<td>- 1.2</td>
</tr>
<tr>
<td>Body fat %</td>
<td>- 0.1</td>
</tr>
<tr>
<td>VAT</td>
<td>+ 8</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>- 22</td>
</tr>
<tr>
<td>Insulin</td>
<td>- 15</td>
</tr>
<tr>
<td>LDL-C</td>
<td>+ 2.7</td>
</tr>
<tr>
<td>TG</td>
<td>+ 2.4</td>
</tr>
<tr>
<td>HDL -C</td>
<td>- 2.5</td>
</tr>
<tr>
<td>Supine SBP</td>
<td>- 6.3</td>
</tr>
</tbody>
</table>

No significant between group or within group differences.
Preliminary data suggests decrease in biomarkers of inflammation after AEX

- Percent Change:
  - IL-6 - 2%
  - TNF-α - 2%
  - IL-8 - 7%
  - hsCRP - 10%

- Trends not statistically significant

- If exclude a subject with baseline hsCRP= 13 mg/L, then hsCRP mg/L mean ± SE:
  - Baseline = 3.5 ± 0.9
  - Post AEX= 2.8 ± 0.8
  - ∆ CRP = -0.7 ± 0.6
Summary: AEX in older HIV +

- Safe and well-tolerated
  - Medical holds due to age-related comorbidity

- Low and high-intensity AEX increased ambulatory function
  - Average increase of 58 meters
  - Gain of ≥50 meters in 70% of patients

- High intensity AEX increased cardiorespiratory fitness
  - Average increase of 17% ~ 1 MET (metabolic equivalent)

- AEX without weight loss did not significantly reduce CVD risk factors.
Future Directions

• Randomized trials to determine the ideal exercise training
  – Can low intensity AEX increase survival and limit disability?
  – Is high-intensity AEX required to overcome the combined negative effects of aging and chronic infection/treatment?
  – How should resistive training be included?

• Mechanistic research to investigate
  – Skeletal muscle mitochondrial function
  – Cardiac function and adaptation to exercise
  – Systemic and tissue inflammatory mediators
1. Aerobic exercise is safe, well-tolerated, and effective in improving ambulatory function in older HIV-infected men.

2. Exercise strategies are needed to target the pathogenesis of aging in HIV, and to generate lifestyle recommendations that are tailored for this patient population.
Acknowledgements

Dedicated Staff & Patients

Mary Bowers-Lash, RN
Walter Williams
Jeff Beans
Troy Stevenson
Danielle Lopinski
Anita Neal, LPN
Cheryl Beasley, LPN
Ivy Doresy, RN

Funding: K23AG024896 (Oursler), University of Maryland OAIC, P60AG12583 (Goldberg) and the Baltimore VA Geriatric Research, Clinical and Education Center