“Metabolic Disorders Associated with HIV/AIDS Disease and Treatment”

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Metabolic Problems Can Be Due To...

1. Immune dysfunction
2. Medication side effects
3. Infection
4. Alterations in the hormonal milieu
5. The effects of HIV itself
6. Physical inactivity
7. Poor dietary habits

Prevalence in the general US population is ~25% (1). The prevalence among persons living with HIV/AIDS is uncertain, but one study suggests the rate is between 14% and 18% depending on the criteria used (2).

In the year 2000, approximately 150 million people worldwide had type 2 diabetes and this figure is expected to double by 2025 (3).

What Characterizes Metabolic Problems?

1. Dyslipidemia with an atherogenic profile (i.e., elevated blood lipids)

2. Altered patterns of body composition (e.g., peripheral loss of fat [lipoatrophy] and central fat deposition [lipohypertrophy])

3. Alterations in carbohydrate metabolism/insulin resistance (i.e., insulin sensitivity or glucose dysregulation)

4. Changes in organ or other tissue function, leading to altered utilization, storage, and excretion of nutrients
What Characterizes Metabolic Problems?

5. Pro-thrombotic state
6. Pro-inflammatory state
7. Bone metabolism alterations
8. Mitochondrial toxicity
9. Lactic acidemia

The prevalence of metabolic and morphologic alterations has increased since the introduction of highly active antiretroviral treatment (HAART).

Knowledge of the various aspects involved in their diagnosis and treatment is necessary for appropriately treating people living with HIV/AIDS.

However, some of these metabolic problems may have occurred independently and before the introduction of antiretroviral treatment (ARV)/HAART (1, 2).


While HAART has Increased Life Span...

New challenges are now being confronted:

1. Lipodystrophy is a complex issue in HIV care.
2. Body composition should be monitored regularly for changes that indicate a decrease in lean body mass.
3. Health care providers should discuss the psychosocial impact of lipodystrophy with the patient.
While HAART has Increased Life Span...

4. Some clients may consider discontinuing HAART treatment because of body image issues.

5. Nutrition interventions should support the client’s medication treatment goals while reducing any negative nutrition-related health impacts of the disease and the medication regimens.

6. Co-infections, such as Hepatitis C, may require specific attention to organ systems and the potential for additional therapies to interact with nutritional status, food, and other medications (1).

Indicators of Cardiovascular (CVD) Risk

CVD risk factors must first be identified to be followed and modified.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male abdominal obesity</td>
<td>Abdominal circumference &gt; 102 cm</td>
</tr>
<tr>
<td>Female abdominal obesity</td>
<td>Abdominal circumference &gt; 88 cm</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥ 150 mg/dl</td>
</tr>
<tr>
<td>Male HDL-C</td>
<td>&lt; 40 mg/dl</td>
</tr>
<tr>
<td>Female HDL-C</td>
<td>&lt; 50 mg/dl</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>≥ 130/85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>≥ 110 mg/dl</td>
</tr>
</tbody>
</table>

### Indicators of Cardiovascular (CVD) Risk

#### Treatment Objectives Based on Risk Categorization.

<table>
<thead>
<tr>
<th>Cardiovascular Prevention</th>
<th>Risk Categorization</th>
<th>Treatment Objective for LDL-C</th>
<th>Treatment Objective for non-HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>&lt; 2 CVRF</td>
<td>&lt; 160</td>
<td>&lt; 190</td>
</tr>
<tr>
<td></td>
<td>≥ 2 CVRF</td>
<td>&lt; 130</td>
<td>&lt; 160</td>
</tr>
<tr>
<td>Secondary</td>
<td>Coronary disease or equivalent</td>
<td>&lt; 100</td>
<td>&lt; 130</td>
</tr>
</tbody>
</table>

Approaches to CVD Treatment

With HIV and ARV/HAART, a high prevalence of CVD risk factors are apparent:

1. The same criteria for managing CVD risk in the general population have been employed with specific nuances.
2. Smoking (tobacco use) should be stopped and second-hand smoke avoided.
3. In patients with dyslipidemia who require drug treatment, statins and/or fibrates are used and increases in blood lipids should be regularly monitored (1).

Approaches to CVD Treatment

4. Diet and exercise should be the first therapeutic recommendation (1, 2).

5. Following a heart-healthy diet and exercise program has been shown to reduce blood lipid levels in HIV-positive patients (3).

6. Clients require support to attain a healthful body weight and to reduce their intake of saturated fat, trans-fatty acids, salt, and dietary cholesterol.

7. Clients with hypertriglyceridemia would benefit from increasing fiber intake, limiting simple carbohydrates, and avoiding alcohol (4).


Approaches to Insulin Resistance

1. Participating in diabetes education programs that can be integrated into routine health care to learn strategies for regulating their blood glucose (1).

2. High fiber, fresh vegetables, elimination of processed foods, and a consistent exercise regimen.

3. Oral anti-diabetic drugs have mixed results. Metformin has shown some promise for the reduction of central fat accumulation, whereas the glitazones are under investigation for their potential to slow or reverse facial and peripheral subcutaneous fat losses (2-4).

4. Other medications may be indicated to help reduce blood lipid levels and insulin resistance and to increase lean body mass.


Approaches to Fat Redistribution

The approach to anomalous fat re-distribution (lypodistrophy) is controversial.

The main approaches at present are:

- Changing ARV medications
- Reparative surgery
- Psychological support
- Lifestyle changes, like exercise and nutritional modification
Approach to Fat Redistribution

Because the wasting process has changed during the HAART era, persons with HIV/AIDS may experience body composition changes, such as lipodystrophy, which are not reflected as weight change and may not be identified in a weight record (1).

Body composition changes characterized as lipodystrophy syndrome may involve fat accumulation in the abdomen, dorsocervical, and breast areas, and subcutaneous fat loss in the limbs and face (2).

**Methods to Assess Fat Redistribution**

Screening and monitoring of wasting, lipodystrophy, and other body changes can be accomplished using measures of body composition, including:

1. **Anthropometrics (weight, skinfold, BMI, waist circumference)**
2. **Bioelectric impedance analysis**
3. **Computed tomography (CT) scans**
4. **Magnetic resonance imaging (MRI)**
5. **Dual energy x-ray absorptiometry (DEXA) scans**

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While these aforementioned techniques can provide data on the patient’s nutritional status and alterations in body dimensions and composition, the clinician should be sensitive to the patient’s body image and self-esteem.

The health care provider and the patient should make informed decisions together about the use of anthropometrics to determine problems and monitor treatment (1, 2).

Changes in Bone Mineral Density (BMD)

Osteopenia, osteoporosis, and osteonecrosis affect patients living with HIV/AIDS.

HAART results in a reduction of BMD.

However, HIV itself likely causes a reduction in BMD according to some research. This process is mediated by cytokines and immune system activation.

The risk of fractures is unknown and it is also unknown how to improve BMD and prevent fractures.

Changes in Bone Mineral Density (BMD)

Osteonecrosis has been reported in HIV-infected patients since 1990 (1), and its incidence appears to be increasing (2).

Available data suggest that corticosteroid use and other risk factors contribute significantly to its pathogenesis.

Improving the understanding of the pathogenesis of these bone disorders should result in better prevention and therapy.

Prevention and early detection are essential, so the use of DEXA would be useful where available.

This issue is especially important for children and peri-menopausal women.

Lactic Acidemia

It is defined by venous lactate > 2.0 mmol/L.

It is common to several toxicities associated with nucleoside analog reverse transcriptase inhibitors (NRTI).

It is usually rare and the only patient group that appears to be at greater risk is pregnant women.

Mild asymptomatic lactic acidemia is common, but it appears to lead to more severe illness only rarely.

The extent of the prevalence, type, diagnosis, and management of illnesses associated with lactic acidosis is unknown.

Lactic Acidemia

Typical measurement of plasma lactate should be limited to patients with previous acidemia who reinitiate NRTI therapy or pregnant women.

For symptomatic lactic acidemia (generally > 5 mmol/L), NRTI and other ARV should be stopped.

Asymptomatic lactic acidemia should not be treated and should not lead to a change in ARV.

Therapies that will reduce the incidence and impact of lactic acidemia are required, as are newer, less toxic NRTIs.

Is Gender an Important Consideration?

Medication interactions may be different for men and women, which may be related to varying hormone and enzyme levels and body composition (1).

For example, women may experience higher increases in blood lipids, whereas the expected differences in ratios between LDL cholesterol and HDL cholesterol disappear between the sexes with ARV.

Is Gender an Important Consideration?

A higher percentage of women experience fat accumulation, whereas men tend to experience subcutaneous fat losses.

In the use of ritonavir- and nelfinavir-containing regimens, men may experience more diarrhea, whereas women may experience nausea, vomiting, and abdominal pain more frequently than men.

Summary

An increase in longevity suggests that both clients and health care professionals will have to address chronic metabolic and physical alterations as a part of routine health care provision for persons living with HIV/AIDS (1).

Summary

Metabolic syndrome prevalence is significant with the HIV/AIDS population and is associated with many co-morbidities.

The metabolic consequences of HAART and HIV itself suggest a heightened risk of CVD, diabetes, bone problems, and others, despite an era where morbidity and mortality have been improved by immune system reconstitution.
Summary

The long-term consequences of metabolic syndrome combined with HAART use offer the clinician and researcher numerous opportunities to improve the lives of persons living with HIV/AIDS.
Thank you for your attention!