Table 15h. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Lipodystrophies and Weight Gain

Updated: Apr.11, 2022
Reviewed: Apr.11, 2022

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/ Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/ Monitoring</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipodystrophy (Fat Maldistribution)</td>
<td>• See below for specific associations.</td>
<td>• Onset</td>
<td>• Frequency is low (&lt;5%) with current regimens.</td>
<td>• Genetic predisposition</td>
<td>Prevention • Initiate a calorically appropriate low-fat diet and an exercise regimen.</td>
<td>• Physicians should perform a regimen review and consider changing the regimen when lipodystrophy occurs.</td>
</tr>
<tr>
<td>General Information</td>
<td></td>
<td>• Increase in trunk and limb fat is the first sign; peripheral fat wasting may not appear for 12–24 months after ART initiation.</td>
<td></td>
<td>• Puberty</td>
<td>Monitoring • BMI measurement • Waist circumference and waist-hip ratio</td>
<td>Improvement in fat maldistribution can vary following a regimen change. Improvement may occur after several months or years, or it may not occur at all.</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• HIV-associated inflammation</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Older age</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Longer duration of ART</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Body habitus</td>
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<tr>
<td>Central Lipohypertrophy or Lipo-Accumulation</td>
<td>• Can occur in the absence of ART, but these conditions most often are associated with the use of PIs and EFV.</td>
<td>• Presentation</td>
<td>• Frequency is low (&lt;5%) with current regimens.</td>
<td>• Obesity before initiation of therapy</td>
<td>Prevention • Initiate a calorically appropriate low-fat diet and an exercise regimen.</td>
<td>• Counsel patient on lifestyle modification and dietary interventions (e.g., maintaining a calorically appropriate diet that is low in saturated fats and simple carbohydrates and starting an exercise regimen, especially strength training).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Central fat accumulation with increased abdominal girth, which may include a dorsocervical fat pad (buffalo hump). Gynecomastia may occur in males, or breast hypertrophy may occur in females, particularly with the use of EFV.</td>
<td></td>
<td>• Sedentary lifestyle</td>
<td>Monitoring • BMI measurement • Waist circumference and waist-hip ratio measurements</td>
<td>• Recommend smoking cessation (if applicable) to decrease future CVD risk.</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Facial/Peripheral Lipoatrophy</th>
<th>Presentation</th>
<th>Prevention</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most cases are associated with the use of ZDV, a thymidine analogue NRTI.</td>
<td>• Thinning of subcutaneous fat in the face, buttocks, and extremities, measured as a decrease in trunk/limb fat by DXA or triceps skinfold thickness. Preservation of lean body mass distinguishes lipoatrophy from HIV-associated wasting.</td>
<td>• Frequency is low (&lt;5%) with current regimens.</td>
<td>• Underweight before ART initiation</td>
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</tbody>
</table>

**Consider using an INSTI instead of a PI or EFV, although some INSTIs may be associated with generalized weight gain (see below).**

**Data Are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children**

- Recombinant human growth hormone
- Growth hormone–releasing hormone
- Metformin
- Thiazolidinediones
- Recombinant human leptin
- Anabolic steroids
- Liposuction

**Facial/Peripheral Lipoatrophy**

- Most cases are associated with the use of ZDV, a thymidine analogue NRTI.

**Presentation**

- Thinning of subcutaneous fat in the face, buttocks, and extremities, measured as a decrease in trunk/limb fat by DXA or triceps skinfold thickness. Preservation of lean body mass distinguishes lipoatrophy from HIV-associated wasting.

**Prevention**

- Limit the use of ZDV.

**Monitoring**

- Patient self-report and physical examination are the most sensitive methods of monitoring lipoatrophy.
<table>
<thead>
<tr>
<th>Weight Gain</th>
<th>Onset</th>
<th>Rate of development of obesity is unclear.</th>
<th>In Infants and Children</th>
<th>Prevention</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Significant weight gain may occur with all ARV regimens, but it appears to be more pronounced with DTG, BIC, and TAF.</td>
<td>• Gradual weight gain after initiating ARV drugs is common with all currently used regimens. The mechanism for weight gain is unclear and under investigation.</td>
<td></td>
<td>• Have not been evaluated yet</td>
<td>• Initiate a calorically appropriate low-fat diet and an exercise regimen.</td>
<td>• BMI measurement</td>
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<tr>
<td>In Adolescents</td>
<td>• Female sex</td>
<td></td>
<td></td>
<td></td>
<td>• Waist circumference and waist-hip ratio measurements</td>
</tr>
<tr>
<td>• Pre-treatment obesity</td>
<td></td>
<td></td>
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<tr>
<td>In Adults</td>
<td>• Low pre-treatment BMI</td>
<td></td>
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<tr>
<td>• Older age</td>
<td>• Female sex</td>
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<tr>
<td>• Black race</td>
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</tbody>
</table>

**Prevention**
- Initiate a calorically appropriate low-fat diet and an exercise regimen.
- Counsel patient on lifestyle modification and dietary interventions (e.g., maintaining a calorically appropriate healthy diet that is low in saturated fats and simple carbohydrates and starting an exercise regimen, especially strength training).

**Monitoring**
- BMI measurement
- Waist circumference and waist-hip ratio measurements

**Key:** ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMI = body mass index; CVD = cardiovascular disease; DTG = dolutegravir; DXA = dual energy X-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; ZDV = zidovudine
See the archived version of Supplement III, February 23, 2009, Pediatric Guidelines on the Clinical info website for a more complete discussion and reference list.
References 1-44


9. de Castro JAC, de Lima LRA, Silva DAS. Accuracy of octa-polar bioelectrical impedance analysis for the assessment of total and appendicular body composition in children and adolescents with HIV: comparison with dual energy X-ray absorptiometry and air
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