Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 15f. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus *(Last updated May 22, 2018; last reviewed May 22, 2018)*

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<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
<th>Estimated Frequency</th>
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<td>Insulin Resistance, Asymptomatic Hyperglycemia, DM</td>
<td>NRTIs: • ZDV • d4T • ddI &lt;br&gt; d4T or ddI are no longer recommended for use in an ARV regimen. &lt;br&gt; PIs: • LPV/r • Rarely other PIs</td>
<td>Onset: &lt;br&gt;• Weeks to months after beginning therapy &lt;br&gt;Presentation: &lt;br&gt;• Asymptomatic fasting hyperglycemia (possibly in the setting of lipodystrophy), metabolic syndrome, or growth delay &lt;br&gt;• Symptomatic DM (rare)</td>
<td>Children: &lt;br&gt;• Insulin resistance, 6% to 12% &lt;br&gt;• Impaired fasting glucose, 0% to 7% &lt;br&gt;• Impaired glucose tolerance, 3% to 4% &lt;br&gt;• DM, 0.2 per 100-child-years</td>
<td>Risk Factors for Type 2 DM: &lt;br&gt;• Lipodystrophy &lt;br&gt;• Metabolic syndrome &lt;br&gt;• Family history of DM &lt;br&gt;• High BMI (obesity)</td>
<td>Prevention: &lt;br&gt;• Lifestyle modification &lt;br&gt;• Do not use d4T or ddI (individually or together); co-administration is contraindicated (no exceptions). &lt;br&gt;• Avoid ZDV when possible.</td>
<td>Counsel on lifestyle modification (e.g., a diet low in saturated fat, cholesterol, trans fat, and refined sugars; increased physical activity; cessation of smoking); recommend consultation with dietician. Change NRTI backbone (e.g., from ZDV, d4T, or ddI to TAF, TDF, or ABC). For Either RPG ≥200 mg/dL plus Symptoms of DM or FPG ≥126 mg/dL: &lt;br&gt;• Patient meets diagnostic criteria for DM; consult endocrinologist. &lt;br&gt;FPG 100–125 mg/dL: &lt;br&gt;• Impaired FPG is suggestive of insulin resistance; consult endocrinologist. &lt;br&gt;FPG &lt;100 mg/dL &lt;br&gt;Normal FPG, but Does Not Exclude Insulin Resistance: &lt;br&gt;• Recheck FPG in 6–12 months.</td>
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*Insulin resistance, asymptomatic hyperglycemia, and DM form a spectrum of increasing severity. Insulin resistance is often defined as elevated insulin levels for the level of glucose observed; impaired FPG as an FPG of 100–125 mg/dL; impaired glucose tolerance as an elevated 2-hour PG of 140–199 mg/dL in a 75 g-OGTT (or if <43 kg, 1.75 g/kg of glucose up to a maximum of 75 g); and diabetes mellitus as either an FPG ≥126 mg/dL, a random PG ≥200 mg/dL in a patient with hyperglycemia symptoms, an HgbA1c of ≥6.5%, or a 2-hour PG after OGTT ≥200 mg/dL. However, the Panel does not recommend routine determinations of insulin levels, HgbA1c, or glucose tolerance without consultation with an endocrinologist. These guidelines are instead based on the readily available RPG and FPG levels.

**Key to Acronyms:** ABC = abacavir; ARV = antiretroviral; BMI = body mass index; d4T = stavudine; ddI = didanosine; dL = deciliter; DM = diabetes mellitus; FPG = fasting plasma glucose; HgbA1c = glycosylated hemoglobin; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; OGTT = oral glucose tolerance test; PG = plasma glucose; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine
References


