Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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### Table 15g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis

(Last updated April 16, 2019; last reviewed April 16, 2019)

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<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
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<td>Lactic Acidosis</td>
<td>NRTIs: • ZDV; • Less likely with 3TC, FTC, ABC, TAF, and TDF</td>
<td>Onset: • Generally, after years of exposure; • Lactic acidosis may be clinically asymptomatic; • Insidious Onset of a Combination of Signs and Symptoms: • Generalized fatigue, weakness, and myalgias; • Vague abdominal pain, weight loss, unexplained nausea, or vomiting; • Dyspnea; • Peripheral neuropathy</td>
<td>Lactic acidosis is associated with use of ddI and d4T. Cases are rare now that these NRTIs are no longer recommended. 3TC, FTC, ABC, TAF, and TDF are less likely to induce clinically significant mitochondrial dysfunction than ZDV.</td>
<td>Adults: • Female sex; • High BMI; • Chronic HCV infection; • African-American race; • Co-administration of TDF with metformin; • Overdose of propylene glycol; • CD4 cell count &lt;350 cells/mm³; • Acquired riboflavin or thiamine deficiency; • Possibly pregnancy.</td>
<td>Prevention: • Due to the presence of propylene glycol as a diluent, LPV/r oral solution should not be used in preterm neonates or any neonate who has not attained a postmenstrual age of 42 weeks and a postnatal age of ≥14 days. • Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy.</td>
<td>Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test): • Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup. Lactate &gt;5.0 mmol/L (Confirmed With a Second Test) or &gt;10.0 mmol/L (Any One Test): • Discontinue all ARV drugs. • Provide supportive therapy (e.g., IV fluids; some patients may require sedation and respiratory support to reduce oxygen demand and ensure adequate oxygenation of tissues). Anecdotal (Unproven) Supportive Therapies: • Administer bicarbonate infusions, THAM, high doses of thiamine and riboflavin, oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C). Following the resolution of clinical and laboratory abnormalities, resume therapy, either with a NRTI-sparing regimen or a revised NRTI-containing regimen. Institute a revised NRTI-containing regimen with caution, using NRTIs that are less likely to induce mitochondrial dysfunction (ABC, TAF, or TDF preferred; possibly FTC or 3TC). Lactate should be monitored monthly for ≥3 months.</td>
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<td>Other Drugs: • See Risk Factors and Prevention/Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates.</td>
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* Blood for lactate determination should be collected, without prolonged tourniquet application or fist clenching, into a pre-chilled, gray-top, fluoride-oxalate-containing tube and transported on ice to the laboratory to be processed within 4 hours of collection.

* Management can be initiated before receiving the results of the confirmatory test.

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BMI = body mass index; CD4 = CD4 T lymphocyte; d4T = stavudine; ddI; didanosine; FTC = emtricitabine; HCV = hepatitis C virus; IV = intravenous; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; THAM = tris (hydroxymethyl) aminomethane; ZDV = zidovudine

*Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*
References

General Reviews


Risk Factors


Monitoring and Management

