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

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

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<th>Adverse Effects</th>
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<td><strong>Lactic Acidosis</strong></td>
<td>NRTIs: d4T and ddI have the highest risk when co-administered, followed by ZDV. d4T or ddI are not recommended in an ARV regimen. 3TC, FTC, ABC, TAF, and TDF are less likely to induce mitochondrial dysfunction of clinical significance.</td>
<td>Onset: 1–20 months after starting therapy (median onset was 4 months in 1 case series) Presentation Usually 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 Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic, pancreatic, respiratory failure).</td>
<td>The following information is based on studies that included d4T and ddI. Chronic, Asymptomatic Mild Hyperlactatemia (2.1–5.0 mmol/L) Adults: 15% to 35% of adults receiving NRTI therapy for &gt;6 months Children: 29% to 32% Symptomatic Severe Hyperlactatemia (&gt;5.0 mmol/L) Adults: 0.2% to 5.7% Symptomatic Lactic Acidosis/Hepatic Steatosis: Rare in all age groups (1.3–11 episodes per 1,000 person-years; increased incidence with the use of d4T/ddI when co-administered), but associated with a high fatality rate (33% to 58%)</td>
<td>Adults: Female sex High BMI Chronic HCV infection African-American race Prolonged NRTI use (particularly d4T and ddI) Co-administration of ddI with other agents (e.g., d4T, TDF, RBV, tetracycline) Co-administration of TDF with metformin Overdose of propylene glycol CD4 count &lt;350 cells/mm² Acquired riboflavin or thiamine deficiency Possibly pregnancy Preterm Infants or Any Neonates before Post-Menstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days has Been Attained</td>
<td>Do not use d4T or ddI (individually or together) in an ARV regimen; co-administration is contraindicated (no exceptions). Due to the presence of propylene glycol as a diluent, LPV/r oral solution should not be used in preterm neonates or any neonate before a postmenstrual age of 42 weeks and a postnatal age of ≥14 days has been attained. Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy. Provide supportive therapy (IV fluids; some patients may require sedation and respiratory support to reduce oxygen demand and ensure adequate oxygenation of tissues). Anecdotal (Unproven) Supportive Therapies: Bicarbonate infusions, THAM, high-dose thiamine and riboflavin, oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C) Following resolution of clinical and laboratory abnormalities, resume therapy, either with a NRTI-sparing regimen or a revised NRTI-containing regimen instituted with caution, using NRTIs less likely to induce mitochondrial dysfunction (ABC, TAF, or TDF preferred; possibly FTC or 3TC), and lactate should be monitored monthly for at least 3 months.</td>
<td></td>
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**a** 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.

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

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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; RBV = ribavirin; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; THAM = tris (hydroxymethyl) aminomethane; ZDV = zidovudine

References

General Reviews

Fatal Lactic Acidosis

Risk Factors


Monitoring and Management


