### Lactic Acidosis

**Onset/Clinical Manifestations**
- **Adults:** 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.**

**Estimated Frequency**
- **Adults:**
  - Female sex
  - High BMI
  - Chronic HCV infection
  - African-American race
  - Coadministration of TDF with metformin
  - Overdose of propylene glycol
  - CD4 cell count <350 cells/mm³
  - Acquired riboflavin or thiamine deficiency
  - Possibly pregnancy

**Prevention/Management**
- **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.

**Monitoring**
- **Asymptomatic Patients:** Measurement of serum lactate is not recommended.
- **Patients with Clinical Signs or Symptoms Consistent with Lactic Acidosis:**
  - Obtain blood lactate level.¹
  - Additional diagnostic evaluations should include serum bicarbonate, anion gap, and/or arterial blood gas; amylase and lipase; serum albumin; and hepatic transaminases.

**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.

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

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

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

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

<table>
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<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
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<th>Prevention/Monitoring</th>
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<tr>
<td>Lactic Acidosis</td>
<td>NRTIs; ZDV; Less likely with 3TC, FTC, ABC, TAF, and TDF</td>
<td>Lactic acidosis is associated with use of ddI and d4T. Cases are rare now that these NRTIs are no longer recommended.</td>
<td><strong>Insidious Onset of a Combination of Signs and Symptoms:</strong></td>
<td><strong>Adults:</strong> Female sex, High BMI, Chronic HCV infection, African-American race, Coadministration of TDF with metformin, Overdose of propylene glycol, CD4 cell count &lt;350 cells/mm³, Acquired riboflavin or thiamine deficiency, Possibly pregnancy</td>
<td><strong>Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test):</strong> Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup. Lactate &gt;5.0 mmol/L (Confirmed With a Second Test)b 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). Ancodotal (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>
<td><strong>Note:</strong> Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure). <strong>Combination of Signs and Symptoms:</strong></td>
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</tbody>
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1. 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.

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

General Reviews


Risk Factors


Monitoring and Management


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