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>
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<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 ddl and d4T. Cases are rare now that these NRTIs are no longer recommended.</td>
<td>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</td>
<td>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.</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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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.

## Lactic Acidosis

**Onset:**
- Generally, after years of exposure
- An 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 failure, pancreatic failure, respiratory failure).

**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.

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

**Management:**
- Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test):
  - Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup.
- Lactate >5.0 mmol/L (Confirmed With a Second Test) or >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.

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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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References

General Reviews


Risk Factors


Monitoring and Management

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