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
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<td>Lactic Acidosis</td>
<td>NRTIs:</td>
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<td></td>
<td>• d4T and ddI have the highest risk when co-administered, followed by ZDV.</td>
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<td>Onset: 1–20 months after starting therapy (median onset was 4 months in 1 case series)</td>
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<td>• d4T or ddI are not recommended in an ARV regimen.</td>
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<td>Presentation: Usually Insidious Onset of a Combination of Signs and Symptoms:</td>
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<td>• 3TC, FTC, ABC, TAF, and TDF are less likely to induce mitochondrial dysfunction of clinical significance.</td>
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<td>Generalized fatigue, weakness, and myalgias</td>
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<td>Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic, pancreatic, respiratory failure).</td>
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<td>Vague abdominal pain, weight loss, unexplained nausea, or vomiting</td>
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<td></td>
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<td></td>
<td>Dyspnea</td>
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<td>Peripheral neuropathy</td>
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</table>

Lactic Acidosis

Onset:

Adults:

- 15% to 35% of adults receiving NRTI therapy for >6 months

Children:

- 29% to 32%

Symptomatic Severe Hyperlactatemia (>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%)

Adul ds:

- 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 <350 cells/mm³
- 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.

- Discontinue all ARVs.
- Prevention: 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.

Monitoring

Asymptomatic:

- Measurement of serum lactate is not recommended.

Clinical Signs or Symptoms Consistent with Lactic Acidosis:

- Obtain blood lactate level.
- Additional diagnostic evaluations should include serum bicarbonate and anion gap and/or arterial blood gas, amylase and lipase, serum albumin, and hepatic transaminases.

Prevention:

- 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.

Management

Lactate 2.1–5.0 mmol/L (Confirmed with Second Test):

- Replace ddI and d4T with other ARVs.
- As an alternative, temporarily discontinue all ARVs while conducting additional diagnostic workup.
- Lactate >5.0 mmol/L (Confirmed with Second Test) or >10.0 mmol/L (Any 1 Test):
  - Discontinue all ARVs.
  - 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.

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

(Last updated May 22, 2018; last reviewed May 22, 2018) (page 2 of 2)

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


