Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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### Table 13g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis

(Last updated April 27, 2017; last reviewed April 27, 2017)

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| Lactic Acidosis | NRTIs, in particular, d4T and ddI (highest risk when co-administered) | **Onset:**
  - 1–20 months after starting therapy (median onset 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
  - Dyspepsia
  - Peripheral neuropathy
**Note:** Patients may present with acute multi-organ failure (e.g., fulminant hepatic, pancreatic, respiratory failure). |
| Chronic, Asymptomatic Mild Hyperlactatemia (2.1–5.0 mmol/L)
  **Adults:**
  - 15% to 35% of adults receiving NRTI therapy for longer than 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 1000 person-years; increased incidence with the use of d4T/ddI when co-administered), but associated with a high fatality rate (33% to 58%)** |
| Adults: |
  - Female gender
  - 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:
  - Exposure to propylene glycol (e.g., present as a diluent in LPV/r oral solution) due to diminished ability to metabolize propylene glycol, thereby leading to accumulation and potential adverse events.
  | Lactate >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, coenzyme Q10, vitamin C)

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References

General Reviews


Risk Factors


**Monitoring and Management**


