Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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### Lactic Acidosis

**Onset/Clinical Manifestations**
- Generally, after years of exposure
- Lactic acidosis may be clinically asymptomatic.
- 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

**Risk Factors**
- 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/Monitoring**
- 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.

**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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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 receiving the results of the confirmatory test.

**Key to Acronyms:**
- 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BMI = body mass index; CD4 = CD4 T lymphocyte; d4T = stavudine; ddl = 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

