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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| Lactic Acidosis                      | NRTIs:          | Onset: 1–20 months after starting therapy (median onset was 4 months in 1 case series)       | The following information is based on studies that included d4T and ddI.             | Adults:      | Do not use d4T or ddI (individually or together) in an ARV regimen; co-administration is contraindicated (no exceptions) | Lactate 2.1–5.0 mmol/L (Confirmed with Second Test):  
|                                      | d4T and ddI have the highest risk when co-administered, followed by ZDV. | Chronic, Asymptomatic Mild Hyperlactatemia (2.1–5.0 mmol/L) | Adults: 15% to 35% of adults receiving NRTI therapy for >6 months | High BMI     | 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. | Replace ddI and d4T with other ARVs.          |
|                                      | d4T or ddI are not recommended in an ARV regimen. | African-American race | Chronic HCV infection | Female sex | Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy. | As an alternative, temporarily discontinue all ARVs while conducting additional diagnostic workup. |
| 3TC, FTC, ABC, TAF, and TDF are less likely to induce mitochondrial dysfunction of clinical significance. | Prolonged NRTI use (particularly d4T and ddI) | African-American race | Co-administration of ddI with other agents (e.g., d4T, TDF, RBV, tetracycline) | High BMI | Provide supportive therapy (IV fluids; some patients may require sedation and respiratory support to reduce oxygen demand and ensure adequate oxygenation of tissues). | Lactate >5.0 mmol/L (Confirmed with Second Test) or >10.0 mmol/L (Any 1 Test): Discontinue all ARVs. |
|                                      | Co-administration of d4T with other agents (e.g., d4T, TDF, RBV, tetracycline) | African-American race | Co-administration of TDF with metformin | African-American race | Bicarbonate infusions, THAM, high-dose thiamine and riboflavin, oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C) | Anecdotal (Unproven) Supportive Therapies: |
|                                      | Co-administration of TDF with metformin | African-American race | Overdose of propylene glycol | Acquired riboflavin or thiamine deficiency | 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. |
|                                      | Overdose of propylene glycol | Acquired riboflavin or thiamine deficiency | CD4 count <350 cells/mm³ | Possibly pregnancy | | |
|                                      | Vague abdominal pain, weight loss, unexplained nausea, or vomiting | Possibly pregnancy | Acquired riboflavin or thiamine deficiency | | | |
|                                      | Dyspnea | Possibly pregnancy | Acquired riboflavin or thiamine deficiency | | | |
|                                      | Peripheral neuropathy | Possibly pregnancy | Acquired riboflavin or thiamine deficiency | | | |
| Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic, pancreatic, respiratory failure). | | | | | | |

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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

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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; 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**


