Acidosis

Lactic Adverse Effects

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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) | 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% | Symptoms:  
- Generalized fatigue, weakness, and myalgias  
- Vague abdominal pain, weight loss, unexplained nausea or vomiting  
- Dyspnea  
- Peripheral neuropathy | Preventive:  
• d4T and ddI should both be avoided individually; co-administration of d4T and ddI is contraindicated (no exception).  
• 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. |
|                 |                 | 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  
- Dyspnea  
- Peripheral neuropathy  
Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic, pancreatic, respiratory failure). | Monitoring  
Management can be initiated before the results of the confirmatory test. | Preventive:  
• 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.  
• 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. | Preventive:  
• 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) |

Following resolution of clinical and laboratory abnormalities, resume therapy, either with an NRTI-sparing regimen or a revised NRTI-containing regimen instituted with caution, using NRTIs less likely to inhibit mitochondria (ABC or TDF preferred; possibly FTC or 3TC), and monthly monitoring of lactate for at least 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; RBV = ribavirin; TDF = tenofovir disoproxil fumarate; THAM = tris (hydroxymethyl) aminomethane

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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.
References

General Reviews


Risk Factors


**Monitoring and Management**


