Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 13i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects

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<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/Monitoring</th>
<th>Management</th>
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<tr>
<td><strong>Urolithiasis/ Nephrolithiasis</strong></td>
<td>ATV, IDV</td>
<td>Onset: Weeks to months after starting therapy&lt;br&gt;Clinical Findings:&lt;br&gt;• Crystalluria, hematuria, pyuria, flank pain, sometimes increased creatinine</td>
<td>ATV-related nephrolithiasis occurs in &lt;10%.&lt;br&gt;IDV-related higher (29%) in children than adults (12.4%)</td>
<td>In adults, elevated urine pH (&gt;5.7)&lt;br&gt;Unknown in children</td>
<td>Prevention:&lt;br&gt;• Maintain adequate hydration.&lt;br&gt;• IDV is not FDA-approved for use in children and should be avoided.</td>
<td>Provide adequate hydration and pain control; consider using alternative ARV. If on IDV, discontinue.</td>
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<td>Renal Dysfunction</td>
<td>TDF</td>
<td>Onset: Variable; in adults, weeks to months after initiation of therapy.&lt;br&gt;• Hypophosphatemia appears at a median of 18 months.&lt;br&gt;• Glucosuria may have onset after a year of therapy.&lt;br&gt;• Abnormal urine protein/osmolality ratio may be an early indicator.</td>
<td>Adults: Approximately 2% with increased serum creatinine&lt;br&gt;Approximately 0.5% with severe renal complications&lt;br&gt;Children: Approximately 4% with hypophosphatemia or proximal tubulopathy; higher with prolonged TDF therapy, in advanced HIV infection or concomitant use of ddI</td>
<td>Risk May Be Increased in Children with:&lt;br&gt;• Age &gt;6 years&lt;br&gt;• Black race, Hispanic/Latino ethnicity&lt;br&gt;• Advanced HIV infection&lt;br&gt;• Hypertension&lt;br&gt;• Diabetes&lt;br&gt;• Concurrent use of ddl or PIs (especially LPV/r), and preexisting renal dysfunction&lt;br&gt;• Risk increases with longer duration of TDF treatment.</td>
<td>Monitor urine protein and glucose or urinalysis, and serum creatinine at 3- to 6-month intervals. For patients taking TDF, some panelists add serum phosphate to the list of routine labs to monitor. In the presence of persistent proteinuria or glucosuria, or for symptoms of bone pain or muscle pain or weakness, also measure serum phosphate. Because toxicity risk increases with duration of TDF treatment, frequency of monitoring should not decrease with time.</td>
<td>If TDF is the likely cause, consider using alternative ARV. TAF has significantly less toxicity than TDF.</td>
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Table 13i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephotoxic Effects
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<td>Elevation in Serum Creatinine</td>
<td>DTG, COBI, RPV</td>
<td>Onset:</td>
<td>Common</td>
<td>N/A</td>
<td>Monitor serum creatinine. Assess for renal dysfunction if serum creatinine increases by &gt;0.4 mg/dL or increases are ongoing with time.</td>
<td>No need to change therapy. Reassure patient about the benign nature of the laboratory abnormality.</td>
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<td>• Within a month of starting treatment</td>
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<td>Presentation:</td>
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<td></td>
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<td>• Asymptomatic. These drugs decrease renal tubular secretion of creatinine, leading to an increase in measured serum creatinine without a true change in eGFR.</td>
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Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; COBI = cobicistat; ddI = didanosine; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; FDA = Food and Drug Administration; IDV = indinavir; LPV/r = boosted lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

References


