Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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# Table 15i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects

*Last updated April 16, 2019; last reviewed April 16, 2019*

<table>
<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>
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| **Urolithiasis/Nephrolithiasis** | ATV, DRV        | Onset: weeks to months after starting therapy  
Clinical Findings: crystalluria, hematuria, pyuria, flank pain, increased creatinine in some cases | ATV-related nephrolithiasis occurs in <10% of patients. | In adults, elevated urine pH (>5.7)  
The risk factors in children are unknown. | Provide adequate hydration and pain control. Consider using another ARV in place of ATV. | Provide adequate hydration and pain control. Consider using another ARV in place of ATV. |

**Renal Dysfunction**

| Adverse Effects | Associated ARVs | Onset: variable; in adults, renal dysfunction may occur weeks to months after initiating therapy.  
Hypophosphatemia appears at a median of 18 months.  
Glucosuria may occur after a year of therapy.  
Abnormal urine protein/osmolality ratio may be an early indicator.  
Presentation: increased serum creatinine, proteinuria, normoglycemic glucosuria  
Increased urinary protein/creatinine ratio and albumin/creatinine ratio | Adults: approximately 2% experience increased serum creatinine levels.  
Approximately 0.5% experience severe renal complications  
Children: approximately 4% experience hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection. | Risk May Increase in Children with the Following Characteristics:  
Aged >6 years  
Black race, Hispanic/Latino ethnicity  
Advanced HIV infection  
Hypertension  
Diabetes  
Concurrent use of PIs (especially LPV/r) and preexisting renal dysfunction  
Risk increases with longer duration of TDF treatment. | Monitor urine protein, urine glucose and serum creatinine at 3-month to 6-month intervals. For patients taking TDF, some Panel members routinely monitor serum phosphate levels.  
Measure serum phosphate if the patient experiences persistent proteinuria or glucosuria, or has symptoms of bone pain, muscle pain, or weakness.  
Because toxicity risk increases with the duration of TDF treatment, do not decrease the frequency of monitoring over time. | If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less toxicity than TDF. |
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<td>Elevation in Serum Creatinine</td>
<td>DTG, COBI, RPV</td>
<td>Onset: • Within a month of starting treatment</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 if increases continue over time.</td>
<td>No need to change therapy. Reassure the patient about the benign nature of the laboratory abnormality.</td>
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Presentation: • Asymptomatic. These drugs decrease renal tubular secretion of creatinine, leading to an increase in serum creatinine levels without a true change in eGFR.

Common Need to distinguish between a true change in eGFR and other causes. A true change may be associated with other medical conditions, the continuing rise of serum creatinine levels over time, and albuminuria.

N/A Monitor serum creatinine. Assess for renal dysfunction if serum creatinine increases by >0.4 mg/dL or if increases continue over time.

No need to change therapy. Reassure the patient about the benign nature of the laboratory abnormality.

Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; COBI = cobicistat; dL = deciliter; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

References


