Mycophenolate-Associated Colitis

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Background

- Mycophenolate mofetil (Cellcept, MMF)
  - Prodrug
  - Usual dose: 1000 mg PO BID q12 h
  - IV formulation available (1:1 conversion)
  - 250 mg capsule (100): $396.29
- Mycophenolate sodium (Myfortic, MPA)
  - Active form
  - Enteric coated (EC)
  - Usual dose: 720 mg PO BID q12 h
  - 360 mg (120): $1219.69

Indications

- Labeled Indications
  - Prophylaxis of organ rejection in renal, cardiac or hepatic transplants
- Unlabeled Indications
  - Bone Marrow Transplant
  - Crohn’s Disease
  - Lupus nephritis
  - Myasthenia gravis
  - Psoriasis
  - Refractory acute GVHD and chronic GVHD
  - Rheumatoid arthritis
  - Refractory autoimmune hepatitis
  - Ulcerative colitis

Disclosure

- I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation

Objectives

- Characterize incidence and timeline of GI side effects with mycophenolate
- Identify strategies for management of mycophenolate GI toxicity and mycophenolate-associated colitis
- Discuss pharmacist’s role in managing GI side effects associated with mycophenolate

Mechanism of Action
Common ADRs

<table>
<thead>
<tr>
<th>System</th>
<th>ADRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>HTN, hypotension, peripheral edema, chest pain, tachycardia</td>
</tr>
<tr>
<td>CNS</td>
<td>Pain, HA, insomnia, fever, dizziness, anxiety</td>
</tr>
<tr>
<td>Derm</td>
<td>Rash</td>
</tr>
<tr>
<td>Endo/Met</td>
<td>Hyperglycemia, hypercholesterolemia, hypermagnesemia, hypokalemia, hypocalcemia, hyperkalemia</td>
</tr>
<tr>
<td>GI</td>
<td>Abdominal pain, nausea, diarrhea, constipation, vomiting, anorexia, dysphagia</td>
</tr>
<tr>
<td>GU</td>
<td>Urine</td>
</tr>
<tr>
<td>Hematol</td>
<td>Leukopenia, anemia, leukocytosis, thrombocytopenia</td>
</tr>
<tr>
<td>Renal</td>
<td>↑ SCR, ↑ BUN</td>
</tr>
<tr>
<td>Other</td>
<td>Infusion</td>
</tr>
</tbody>
</table>

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- **Diagnosis:**
  - Absence of any other etiology for GI symptoms
  - Resolution of the diarrhea with discontinuation of mycophenolate
  - Presence of typical histopathological changes on colonoscopy

- **Mechanism of colonic injury remains unclear**
  - Immunosuppressive effects may indirectly affect lymphocytes in colon resulting in mucosal protection
  - Direct MMF colonic cytotoxicity cannot be ruled out

- **Management**
  - Discontinuation of mycophenolate

Summary

- Mycophenolate can induce diarrhea weeks to months after initiation
- Mycophenolate-induced colitis should be considered if strategies to reduce diarrhea provide no benefit
- Discontinuation or reduction of MMF dose will usually result in improvement of diarrhea

GI Upset versus Colitis

- Up to 53% of patients report GI symptoms
- Diarrhea is most frequently reported side effect
  - Typical onset: 2-4 weeks after start of therapy (variable)
  - Various strategies to alleviate diarrhea
  - Peak-related
  - Monitoring of levels not routinely recommended
- Mycophenolate-associated colitis
  - Diarrhea still present despite attempted strategies
  - Absence of any alternative cause of diarrhea

Treatment Strategies

- Ensure patient is taking with food
- Divide dose
  - Ex. MMF 500 mg PO QID
- Reduce dose
  - Ex. decrease from 2g/day to 1g/day
- Switch to MPA if using MMF
  - Improved GI tolerability with MPA debatable
- Switch to alternative agent

Pharmacist’s Role

- Inform patients of major side effects, including GI side effects, associated with mycophenolate
- Educate patients and providers regarding strategies to help alleviate diarrhea
- Alert patient or physician if diarrhea continues despite multiple strategies
- If mycophenolate-associated colitis is diagnosed, report to FDA MedWatch
References


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