Aspirin Desensitization for Aspirin-Exacerbated Respiratory Disease (AERD)

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AERD - Description

• Also known as Samter’s Triad
• Refers to the combination of:
  • Asthma
  • Chronic rhinosinusitis (CRS) with nasal polyposis (NP)
  • Acute reactions to aspirin and other COX-1 inhibiting NSAIDs
    • Causing upper and lower respiratory symptoms
• Prevalence:
  • 7% among patients with asthma
  • 15% among patients with severe asthma
  • 9-10% among patients with NP or CRS
  • Up to 30% of asthmatics with NP

• Pathophysiology: Not fully understood but involves dysregulation in arachidonic acid metabolism
  • **Overproduction of Leukotrienes**

![Diagram showing the pathway of leukotrienes and cyclooxygenase (COX) inhibition](image-url)

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AERD - Clinical Features

- **Chronic upper and lower respiratory disease (CRS w/ NP, Asthma) and reaction to NSAIDs is an exacerbating factor.**
- Worsening of asthma and chronic sinusitis occurs even with NSAID avoidance
- Usually diagnosed in adulthood
- The 3 components tend to develop serially over years
- Acute exacerbation after ingestion of NSAID *typically begins 30 minutes to 3 hours after ingestion*
  - Dose-related: small doses produce milder symptoms; large doses produce more severe symptoms
  - Urticaria and/or angioedema occur in 15% of AERD patients.
  - (Similar symptoms may occur with high doses of acetaminophen)
AERD - Diagnosis & Management

- **Diagnosis** made clinically; may require a diagnostic aspirin challenge

- **Management**: Medications, Surgery (polypectomy), *Aspirin Desensitization*
  - *Leukotriene modifying agents* (montelukast, zafirlukast, zileuton)
    - Protect patients from severe exacerbations due to accidental NSAID exposure
    - NSAID avoidance (unless patient has been desensitized to aspirin)

- **Aspirin Desensitization**: Induces one’s ability to temporarily tolerate aspirin. After successful desensitization, the patient must continue aspirin/NSAID daily in order to maintain the desensitized state.
  - **Indications**:
    - Nasal polyposis that worsen or recur after surgery despite optimal medical management
    - Other conditions requiring daily use of NSAIDs (e.g. CAD, arthritis)
  - Reduces the expression of leukotrienes
  - Successful in majority of AERD patients
Aspirin Desensitization

• If sinus surgery/polypectomy is required, schedule desensitization 2-4 weeks after surgery.

Within 1-2 weeks prior to desensitization:
• FEV1 > 70% predicted (optimally)
• Start or continue leukotriene modifier and other asthma medications
• Systemic steroid burst if necessary

Day of Procedure:
• Obtain informed consent, baseline vital signs and spirometry
• Vital Signs, FEV1 (or peak flow) and clinical assessment prior to each dose and with symptoms
• Treatment of reactions (ocular, nasal, laryngeal, bronchial, cutaneous): antihistamines, albuterol, epinephrine
• Lower resp. tract reaction: 15% decrease in the FEV1 from baseline FEV1
• After successful desensitization, start daily aspirin 650 mg twice daily
  • Taper over 6 months to 325 mg twice daily
• Subsequent desensitization is performed if aspirin is missed for more than 48 hours

Protocol

<table>
<thead>
<tr>
<th>Time</th>
<th>Aspirin dose</th>
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<tbody>
<tr>
<td>0</td>
<td>20.25 mg</td>
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<tr>
<td>1.5 hours</td>
<td>40.5 mg</td>
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<tr>
<td>3.5 hours</td>
<td>81 mg</td>
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<tr>
<td>5.5 hours</td>
<td>162 mg</td>
</tr>
<tr>
<td>7.5 hours</td>
<td>325 mg</td>
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</tbody>
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- Most take 2 days. May adjust doses and extend dosing interval based on patient history and assessment.
- If reaction occurs, observe patient for at least 3 hours.
- When stabilized, repeat provoking dose; escalate if tolerated. (Provoking dose is usually 81 mg.)
AERD - Summary

• AERD is a distinct and important subtype of asthma and polypoid sinus disease.

• Early identification is important given the increased morbidity and costs associated with asthma exacerbations and recurrent sinus surgeries.

• Benefits of Aspirin Desensitization followed by daily aspirin in AERD:
  • Decrease in nasal polyp formation, nasal congestion, sinus infections, sinus surgery, and need for systemic corticosteroids
  • Increase in asthma control and sense of smell
  • Effects on CRS symptoms are more dramatic than effects on asthma

References
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