Diagnostic Evaluation in Aspirin-Exacerbated Respiratory Disease

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KEYWORDS

• Aspirin-exacerbated respiratory disease • Diagnosis • NSAID hypersensitivity
• Chronic rhinosinusitis with nasal polyps • Asthma • Intranasal ketorolac
• Oral aspirin challenge • Lysine-aspirin

KEY POINTS

- The diagnosis of aspirin-exacerbated respiratory disease (AERD) is based on the history and confirmed by nonsteroidal anti-inflammatory drug (NSAID) provocation challenge.
- Options for diagnostic challenge include lysine-aspirin challenge by intranasal or inhalation (not available in the United States), oral aspirin challenge, and intranasal ketorolac and modified oral aspirin challenge.
- Oral aspirin challenge is considered the gold standard for diagnosis of AERD.
- Positive provocation challenges result in respiratory and systemic reactions of varying degrees of severity requiring close monitoring and treatment.
- Positive provocation challenges are usually performed as the initial step to NSAID desensitization.

INTRODUCTION

Aspirin-exacerbated respiratory disease (AERD) is widely accepted as a distinct clinical disease, characterized classically by the triad of chronic hyperplastic, eosinophil-rich rhinosinusitis with nasal polyps; asthma; and hypersensitivity reactions to inhibitors of cyclo-oxygenase 1 enzyme (COX-1), such as nonsteroidal anti-inflammatory drugs (NSAIDs). Distinguishing the clinical triad of AERD from other phenotypes of chronic rhinosinusitis with nasal polyps (CRSNP), asthma, and NSAID reactivity is very important for 2 main reasons.

First, patients with AERD are at risk of experiencing very distressing and even life-threatening reactions following ingestion of NSAIDs. In cases of uncertainty regarding

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tolerance of NSAIDs, patients with AERD would need to be counseled that future ingestion of NSAIDs could result in serious reactions, whereas individuals with CRSNP and/or asthma who do not have AERD should not be unduly restricted from taking these NSAIDs when clinically indicated for anti-inflammatory, analgesic, or cardiovascular benefit.

Second, there are treatment modalities uniquely beneficial in patients with AERD as compared with other phenotypes of CRSNP and asthma. As noted elsewhere in this journal, treatment with antileukotriene therapy and long-term treatment with aspirin following aspirin desensitization can have significant therapeutic benefit in AERD.

Although establishing the diagnosis of AERD is important for a number of reasons, making an accurate diagnosis can be challenging. This article is intended to assist the clinician in using the medical history and clinically available diagnostic modalities to accurately identify those patients with AERD, so that they may benefit from the therapies useful in this condition.

DIAGNOSTIC UTILITY OF THE CLINICAL PRESENTATION

The diagnosis of AERD is suggested based on the clinical presentation and confirmed when an individual with a history suggestive of AERD has a clinically observed reaction to aspirin or another NSAID administered by 1 of 3 routes: intranasal, inhalation, or oral ingestion (oral aspirin challenge [OAC]).

Awareness of the prevalence of AERD in patients with CRSNP and asthma can be helpful in the approach to diagnosing AERD. Estimates of the prevalence of AERD in individuals with asthma, CRSNP, or both vary widely depending on the disease severity and means of diagnosis. A recent meta-analysis of several epidemiologic studies found the prevalence of AERD in certain populations to be

- 7% asthma
- 15% severe asthma
- 10% nasal polyps
- 9% unspecified chronic rhinosinusitis[1]

Although the history is helpful in making the diagnosis of AERD, it should not be relied on exclusively. Many patients with AERD may not be aware of their NSAID hypersensitivity. The onset of the reaction can be delayed by 2 to 3 hours after NSAID ingestion, making it difficult for the patient to make the connection between NSAID ingestion and any sudden increase in respiratory symptoms. Some patients with CRSNP and asthma may not have an occasion to take NSAIDs after the onset of disease, whereas others may have been advised to avoid NSAIDs before NSAID intolerance is suggested or confirmed. A European study reported that 15% of patients confirmed to have AERD after a positive challenge were not aware of their NSAID hypersensitivity before challenge.[2]

Dursun and colleagues[3] examined the value of the history provided by the patient in the diagnosis of AERD. In this study involving 243 patients with asthma and CRSNP referred for OAC, prechallenge data were collected from patient recall and available medical records regarding the details of the clinical history, including number and severity of NSAID-induced reactions before presentation. Of the 12 patients who had always avoided NSAIDs, and therefore did not know if they could tolerate taking NSAIDs, 5 (42%) had a positive challenge. The chance of a positive OAC if the patient had at least 1 suspected NSAID reaction was 86%. Patients with 2 or more prior NSAID-induced reactions had an 89% chance of having a positive OAC. In patients with at least 1 severe reaction (defined as a poor response to albuterol and requiring