
Aspirin challenge and desensitization for aspirin-exacerbated respiratory disease: a practice paper

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Aspirin desensitization is indicated for patients who have aspirin-exacerbated respiratory disease and whose asthma and/or rhinosinusitis is suboptimally controlled with inhaled corticosteroids and leukotriene-modifying drugs. In this practice paper, the general requirements for aspirin desensitization are presented, the locations where desensitizations can be safely performed are outlined, prechallenge patient preparation is discussed, an oral aspirin challenge protocol is presented, treatment of adverse reactions is reviewed, and maintenance of aspirin desensitization is discussed.

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INTRODUCTION

Aspirin desensitization is indicated for patients who have aspirin-exacerbated respiratory disease (AERD) and whose asthma and/or rhinosinusitis is suboptimally controlled with inhaled corticosteroids and leukotriene-modifying drugs.^{1–3} This procedure may be considered for individuals who have required multiple polypectomies for nasal polyp control. Patients can be identified as having AERD only after experiencing a respiratory reaction to aspirin or any of the nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit cyclooxygenase-1.⁴ Aspirin desensitization may also be indicated in individuals who require antiplatelet therapy with other cyclooxygenase-1 inhibitors.⁵ Aspirin desensitization may be possible for individuals without AERD but with histories of cutaneous reactions to aspirin or other NSAIDs but is beyond the scope of this article. Patients with cutaneous reactions to aspirin and NSAIDs are a heterogeneous group and may require different desensitization protocols. In AERD patients, an outpatient or inpatient location for desensitization must be determined, but the methods are the same.

GENERAL REQUIREMENTS FOR ASPIRIN DESENSITIZATION

Aspirin desensitization should be performed in a facility able to provide advanced cardiac care, ventilator support, and constant observation by qualified personnel. The supervising physician must be immediately available and should be present at the bedside at the time of the first challenge and through the first reaction. The first reaction is almost always the most severe and is unpredictable. If the first reaction could have been managed without physician intervention, then subsequent challenges may proceed without the supervising physician being physically present.

DESENSITIZATION LOCATION

Inpatient desensitization should be used for patients with the following risk factors: β -blocker use, recent myocardial infarction, any other underlying medical condition or drug treatment regimen that would make the management of severe asthma or anaphylactoid reaction difficult, severe asthma, and history of severe or life-threatening aspirin or NSAID reaction. Outpatient desensitization may be considered when the following conditions exist. The first condition is when a physician experienced in assessing and treating patients with acute, severe asthma exacerbations is immediately available for patient evaluation and treatment. The second condition is when medically qualified personnel experienced in assessing and treating patients with acute, severe asthma exacerbations are available to monitor the patient. Depending on the specific licensing criteria and the scope of practice limitations in a particular state, this could include registered nurses, nurse practitioners, physician assistants, respiratory therapists, and/or other personnel. The third condition is when at least one experienced staff member is solely dedicated to the care and evaluation of the individual patient being desensitized for the full course of the desensitization. The fourth condition is that equipment must be available for

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continuous respiratory and cardiovascular monitoring, pulse oximetry, spirometry, and cardiopulmonary resuscitation.

Asthmatic patients being considered for outpatient aspirin challenge and desensitization should have stable, mild to moderately severe asthma that is well controlled with controller medications and require only occasional use of short-acting β -agonists. Most aspirin desensitizations in individuals with a history of AERD result in significant reactions, and significant life-threatening reactions should be expected. Individuals with negative aspirin challenges do not have AERD.⁶

PRECHALLENGE PROCEDURES

One week before challenge, the following steps should be performed to determine airway stability and optimize asthma therapy. First, obtain spirometry within 1 week of challenge. If the forced expiratory volume in 1 second (FEV₁) is more than 70% of the patient's prior best (and >1.5 L absolute), the patient may be a candidate for outpatient desensitization. Many individuals with AERD often have severe asthma and cannot attain an FEV₁ of 70% when not taking short-acting bronchodilators. These patients need to have inpatient desensitization. Second, within 1 week before challenge, measure FEV₁ every hour for 3 hours and document variability of less than 10%. Third, start dual-controller therapy if poorly controlled asthma is present (long-acting β -agonist and high-dose inhaled steroid). Fourth, consider starting or continuing leukotriene-modifying drug therapy. Fifth, discontinue use of antihistamines 48 hours before challenge. This is necessary to be able to observe a naso-ocular reaction and confirm aspirin sensitivity. Some patients with a history of nasal polyps and asthma will have a negative aspirin challenge. Sixth, use or adjust oral steroid therapy as necessary to achieve adequate airway stability. If the patient is already taking regular systemic steroids, consider doubling the daily maintenance dose. Consider converting every-other-day oral steroid users to every day until the desensitization is complete.

ORAL ASPIRIN CHALLENGE PROTOCOL

For oral aspirin challenge, it is important to discuss the risks and benefits of the procedure with the patient and document the discussion in the medical record. Advise the patient that the procedure may take several days to complete. Obtain written informed consent. Begin early in the morning, and establish intravenous access. Give 20.25 mg of aspirin by mouth followed by 40.5, 81, 162.5, and 325 mg at 90-minute intervals. (Since many practitioners have no access to anything but commercially available aspirin, the dosing is based on using 81-mg aspirin tablets and using a pill cutter to obtain the lower doses. Although almost no one reacts to 20.25 mg, an occasional reaction occurs at 40.5 mg.) Measure the FEV₁ and perform a clinical evaluation at least every 90 minutes and/or with any symptoms. Based on individual patient characteristics, the dosing interval may be extended to 3 hours. A lower respiratory tract reaction is defined as a 15% decrease in the FEV₁ from baseline FEV₁. Record any change in

baseline naso-ocular symptoms. Reactions will likely occur with one of the early doses, usually 81 mg. If it does, treat the reaction with the appropriate medication(s) described herein. When the patient is completely stabilized after a reaction, but not less than 3 hours after the last dose, the provoking dose can be repeated. When the provoking dose is tolerated, dose escalation may continue. A persistent, greater than 15% decrease in FEV₁, with or without other associated symptoms lasting longer than 3 hours despite therapy, is an indication to discontinue the desensitization process for the day. Start the second day of the desensitization process by repeating the last tolerated dose. Continue the desensitization procedure as indicated herein until the goal of tolerating 325 mg of aspirin is reached. Most individuals will take 2 days to complete the desensitization procedure.⁷

ADVERSE REACTION TREATMENT PROTOCOLS

For isolated pulmonary symptoms, have an albuterol metered-dose inhaler with a spacer tube or a hand-held nebulizer with albuterol prepared and ready to deliver. Have the patient inhale up to 5 breaths. Aspirin-induced reactions can last for several hours. Repeat the treatment as necessary. For laryngeal symptoms, use racemic epinephrine in a hand-held nebulizer and/or intramuscular epinephrine. For laryngeal edema with hypotension, use intramuscular epinephrine. For isolated hypotension, use intramuscular epinephrine. For ocular and/or nasal reactions, use oral antihistamines. For urticaria or angioedema, use oral or intravenous antihistamines. Follow the anaphylaxis practice parameter for treatment of anaphylaxis, specific dosing recommendations, and general adverse reaction management.⁸

MAINTENANCE

Aspirin is typically given at 650 mg twice daily after initial desensitization, but many patients can continue maintenance therapy at 325 mg twice daily.⁹⁻¹¹ Tapering can be attempted if the patient is doing well 6 months after beginning desensitization. The desensitized state can be maintained with as little as 81 mg for patients who only need cardiovascular disease prophylaxis. Some people receiving maintenance therapy with 81 mg/d will react when given higher doses of aspirin or other NSAIDs. If the need for higher-dose aspirin or other NSAID use is anticipated, continue maintenance therapy with at least 325 mg/d. It is strongly recommended that subsequent desensitization be performed if aspirin is missed for more than 48 hours.

CONCLUSION

Aspirin desensitization can be safely performed by physicians trained in desensitization protocols, specifically board-certified allergist-immunologists. Aspirin desensitization can provide substantial benefit to patients with AERD. Although respiratory reactions to aspirin are induced during desensitization, no deaths have been reported by any of the authors performing desensitizations in this report.

REFERENCES

1. Berges-Gimeno MP, Simon RA, Stevenson DD. Long-term treatment with aspirin desensitization in asthmatic patients with aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol*. 2003;111:180–186.
2. Fahrenholz JM. Natural history and clinical features of aspirin-exacerbated respiratory disease. *Clin Rev Allergy Immunol*. 2003;24:113–124.
3. Mardiney M, Borish L. Aspirin desensitization for chronic hyperplastic sinusitis, nasal polyposis, and asthma triad. *Arch Otolaryngol Head Neck Surg*. 2001;127:1287.
4. Szczeklik A, Nizankowska E, Duplaga M. Natural history of aspirin-induced asthma. *Eur Respir J*. 2000;16:432–436.
5. Gollapudi RR, Stevenson DD, Simon RA, Teirstein PS. Aspirin sensitivity: Implications for patients with coronary artery disease. *JAMA*. 2004;292:3017–3023.
6. Morwood K, Gills D, Smith W, Kette F. Aspirin-sensitive asthma. *Intern Med J*. 2005;35:240–246.
7. Cormican LJ, Farooque S, Altmann DR, Lee TH. Improvements in oral aspirin challenge protocol for the diagnosis of aspirin hypersensitivity. *Clin Exp Allergy*. 2005;35:717–722.
8. American Academy of Allergy, Asthma & Immunology, American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters. The diagnosis and management of anaphylaxis: an updated practice parameter. *J Allergy Clin Immunol*. 2005;115:S483–S523.
9. Pleskow WW, Stevenson DD, Mathison DA, Simon RA, Schatz M, Zeiger RS. Aspirin desensitization in aspirin-sensitive asthmatic patients: clinical manifestations and characterization of the refractory period. *J Allergy Clin Immunol*. 1982;69:11–19.
10. Zeiss CR, Lockey RF. Refractory period to aspirin in a patient with aspirin-induced asthma. *J Allergy Clin Immunol*. 1976;57:440–448.
11. Lee JA, Simon RS, Stevenson DD. Selection of aspirin doses for aspirin desensitization in patients with aspirin exacerbated respiratory track disease. *J Allergy Clin Immunol*. In press.

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