Aspirin Desensitization: Faster Protocols for Busy Patients

Andrew A. White, MD, and Donald D. Stevenson, MD  San Diego, Calif

In a patient with aspirin-exacerbated respiratory disease (AERD), aspirin desensitization and cross-desensitization with antipyrine were reported in 1922. However, it was not until 1980 that a therapeutic use for daily aspirin treatment, after desensitization, was discovered. The effectiveness of this treatment has been confirmed in patients with AERD at numerous centers, all of which measured improvement in rhino-sinus outcomes. Improvements in asthma outcomes were documented in some, but not in all studies. In the last 38 years, details of aspirin desensitization, followed by daily aspirin treatment, have evolved to the point where this therapeutic intervention is accepted as the standard of care for patients with AERD.

The process of identifying patients with AERD involves 3 steps: (1) AERD only occurs in patients who have rhinosinusitis and asthma; (2) a careful nonsteroidal anti-inflammatory drug (NSAID) exposure and reaction history; and (3) a positive oral aspirin challenge. If the patient gives a history of ingesting a (NSAID) exposure and reaction history; and (3) a positive oral aspirin challenge increase to 89%. No funding was received for this work.

Division of Allergy, Asthma and Immunology, Scripps Clinic, San Diego, Calif. 92130. E-mail: white.andrew@scrippshealth.org.


© 2018 American Academy of Allergy, Asthma & Immunology

https://doi.org/10.1016/j.jaip.2018.10.019
Pelletier et al\textsuperscript{15} present a retrospective observational study of 2 groups of patients with AERD. A baseline group of 16 patients with 90-minute intervals between oral aspirin challenges was contrasted with a new group of 38 patients with 60-minute intervals between escalating doses. Doses of aspirin (diluted Alka-Seltzer), used for both groups, were 40, 80, 160, and 325 mg (skipping the 60 mg dose used in prior protocols). All reactions occurred after the 80 mg dose of aspirin. Both groups provided similar historical information with elapse times from dosing to reactions of <36 minutes. For the 90-minute group, aspirin-provoked reactions occurred at 39 minutes, and for the 60-minute interval group, at 46 minutes. All reactions occurred with intervals well within the 60 minutes. Extreme bronchospastic responses never occurred in either group. When you look at the minimal recorded declines in forced expired volume in 1 second values during aspirin-induced reactions, respiratory safety is obvious for the 16 and 38 reported patients.

However, outliers occur and larger studies will be necessary to incorporate delayed or severe reactions. Equally concerning, the authors reported a desensitization failure rate of 3 patients (18.8\%) in the 90-minute group and 5 (13.3\%) in the 60-minute group. The reader is not provided any details about these 8 of 54 (15\%) patients who failed aspirin desensitization. In our experience, failure to achieve acute desensitization is very uncommon. We recently reported safety outcomes for 167 consecutive aspirin desensitization procedures using our ketorolac/oral aspirin protocol. We identified 23 of 167 (14\%) patients with severe reactions that required multiple dosing before aspirin desensitization was completed. Yet, all 167 subjects advanced to a dose of 325 mg of aspirin, without symptoms, and thus achieved the state of aspirin desensitization. For the 167, the average time to completion of desensitization was 1.67 days, but the subgroup of patients with gastrointestinal reactions averaged 2.29 days. All 167 patients left the clinic taking daily aspirin treatment.\textsuperscript{16} The inability to successfully complete aspirin desensitization might be due to patient decision to stop the challenges or secondary to the speed of the protocol itself. Patients should be warned that a faster protocol might be associated with the disadvantage of not completing aspirin desensitization and/or that further days may be needed to complete desensitization. We suggest that "failure to desensitize" should be a primary endpoint in studies claiming improved protocol variations, not only in this but future protocols.

In a second study, DeGregorio et al\textsuperscript{17} presented their outcomes with the use of a 90-minute dosing interval intended to complete the desensitization in 1 clinic day. Their study included challenge doses of 40.5, 81, and 161 and a mandatory 3-hour observation after onset of reactions. This addition is important, as most studies reporting desensitization protocols do not include the time necessary to treat the inevitable reactions. This study included a typical AERD population without regard to reaction type or timing. One of the 44 subjects could not be desensitized and 2 other patients required a second day to complete desensitization. Thus, the majority (93\%) were able to complete desensitization in 1 day with 1 failure in a gastrointestinal reactor. This study is to be commended for completing desensitization in 43 of 44 patients. An important difference with this protocol, compared with other 90-minute protocols, is that the first dose was 40.5 mg, advancing to 81 mg for the second dose.

In addition, the protocol ended after the patient repeated the provocative dose and tolerated 1 subsequent escalated dose. Thus, the protocol could end before 325 mg of aspirin was administered. These adjustments made it feasible to plan on a 1-day aspirin challenge/desensitization for almost all patients. Although this is an attractive option for patients, the average time to completion was 9.5 hours. If the first dose were administered at 8 am, the average patient would not be discharged until 5:30 PM with some patients requiring 12 hours. Some outpatient clinics might be unable to monitor and staff the procedure properly with this potential obligation. Nonetheless, the point that the procedure can be safely and successfully completed in 1 clinic day is impressive and clearly deserves application to a larger cohort of potential patients with AERD.

As AERD gains a foothold in the diagnostic mainstream, more referrals and desensitization centers for aspirin challenge and desensitization will be needed. An estimation of 1,368,000 patients with AERD in the United States is probably low, given the fact that typical patients are ignored or overlooked.\textsuperscript{18} The demand for oral aspirin challenge centers to diagnosis and treat AERD is already needed and increasing. Safety, reduction of symptoms during reactions, and time to completion for all challenged patients continue to drive innovations in new protocols.

REFERENCES


