



Letter

Desensitization to acetazolamide in a patient with previous antimicrobial sulfonamide allergy

Acetazolamide is a carbonic anhydrase inhibitor that is frequently used in the management of idiopathic intracranial hypertension. Acetazolamide is a sulfonamide agent; specifically, it is a non-sulfonylarylamine, which lacks the amine moiety found at the N4 position that is seen in sulfa antibiotics.¹ Sulfonamide antibiotics contain a substituted ring at the N1 position that is thought to be the driving factor in immediate hypersensitivity reactions.² Although sulfa allergies are commonly reported, there is no evidence to suggest cross-reactivity between sulfonamide antibiotics and sulfonamide nonantibiotics. However, patients can report a history of allergy to both categories of drugs. We present a rapid desensitization protocol to acetazolamide in a patient with history of immediate hypersensitivity reactions to both a sulfonamide antibiotic and acetazolamide.

Our patient is a 21-year-old woman with a history of idiopathic intracranial hypertension who was referred to our clinic by her neuro-ophthalmologist. Her allergic history was significant for development of a pruritic rash after taking 1 week of trimethoprim-sulfamethoxazole a few years before presentation. She had initially been treated with acetazolamide therapy for 1½ years, which was later discontinued and replaced with topiramate, which she tolerated without adverse effect. However, because of suboptimal results after 8 months of topiramate, the patient was again transitioned back to acetazolamide. Within 30 minutes of the first dose of acetazolamide, she developed stomach cramps and urticaria, which responded to diphenhydramine. Acetazolamide treatment was discontinued, and she was subsequently referred for allergy evaluation. Because of the subsequent failure of alternative therapies, including nonmedical management, and after discussion with her neuro-ophthalmologist, the

decision was made to proceed with desensitization to acetazolamide.

We formulated a 12-step intravenous protocol that was performed in the intensive care unit setting (Table 1). Informed consent was provided by the patient, and she tolerated the procedure well without any adverse reactions. The desensitization procedure took 395 minutes or approximately 6.5 hours. She was monitored overnight in the hospital and was observed the following morning after taking 500 mg of acetazolamide orally to ensure tolerance. She was thereafter able to continue her recommended dose of acetazolamide without any issues to date.

The risk of a patient with sulfonamide antibiotic allergy reacting to acetazolamide is rare; only a few occurrences have been documented. The literature generally supports the notion that patients with a history of sulfonamide antibiotic allergy will tolerate sulfonamide nonantibiotics. Tzanakis et al³ described a patient with hypersensitivity to sulfonamides who developed anaphylactic shock after a single dose of acetazolamide. Lee et al⁴ historically reviewed 34 patients with sulfa allergy and intracranial hypertension who received acetazolamide; 2 developed hives, and the remainder had predictable adverse reactions, such as paresthesias. Alternatively, Platt and Griggs¹ described 3 patients with a history of sulfonamide antibiotic who subsequently received acetazolamide with no adverse reaction.

To date, there have been no documented attempts to perform desensitization to acetazolamide. The 12-step drug desensitization protocol used in our case has been described in detail by Castells et al⁵ with regard to use in patients with allergic reactions to chemotherapeutic agents. As with all desensitization procedures, care must be taken to avoid lapses in therapy; significant lapses,

Table 1
Twelve-Step Desensitization Procedure for Acetazolamide

Step	Solution	Rate, mL/h	Time, min	Volume infused per step, mL	Dose administered per step, mg	Cumulative dose administered per step, mg
1	1	2	15	0.5	0.010	0.010
2	1	5	15	1.25	0.025	0.035
3	1	10	15	2.5	0.05	0.085
4	1	20	15	5	0.1	0.185
5	2	5	15	1.25	0.25	0.435
6	2	10	15	2.5	0.5	0.935
7	2	20	15	5	1	1.935
8	2	40	15	10	2	3.935
9	3	10	15	2.5	5	8.935
10	3	20	15	5	10	18.935
11	3	40	15	10	20	38.935
12	3	60	230.5	230.5	461	500

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often greater than 48 hours, would require repeat desensitization. The patient has since been able to successfully continue her dose of acetazolamide without adverse reactions.

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References

- [1] Platt D, Griggs RC. Use of acetazolamide in sulfonamide-allergic patients with neurologic channelopathies. *Arch Neurol*. 2012;69:527–529.
- [2] Brackett C, Singh H, Block J. Likelihood and mechanisms of cross-allergenicity between sulfonamide antibiotics and other drugs containing a sulfonamide functional group. *Pharmacotherapy*. 2004;24:856–870.
- [3] Tzanakis N, Metzidaki G, Bouros D. Anaphylactic shock after a single oral intake of acetazolamide [letter]. *Br J Ophthalmol*. 1998;82:584–588.
- [4] Lee A, Anderson R, Kardon R, et al. Presumed “sulfa allergy” in patients with intracranial hypertension treated with acetazolamide or furosemide: cross-reactivity, myth, or reality? *Am J Ophthalmol*. 2005;138:114–118.
- [5] Castells MC, Tennent NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: outcomes and safety of rapid desensitization in 413 cases. *J Allergy Clin Immunol*. 2008;122:574–580.