
Oral desensitization to 5-aminosalicylic acid medications

MAJ Robert C Stelzle, MD* and COL Edward N Squire, MD

Background: Although hypersensitive subjects have been desensitized to oral sulfasalazine, the feasibility of oral desensitization to the drug's active moiety, 5-aminosalicylic acid has been questioned and never been reported.

Methods: We devised a 5-aminosalicylic acid desensitization protocol and administered the drug to two hypersensitive subjects on three occasions.

Results: Both 5-aminosalicylic acid hypersensitive subjects were successfully desensitized without complications and were able to tolerate therapeutic doses.

Conclusion: Despite changing the drug's properties by crushing it for incrementally increasing administration, we successfully desensitized two patients on three occasions with 5-aminosalicylic acid.

Ann Allergy Asthma Immunol 1999;83:23-24.

INTRODUCTION

Sulfasalazine is a well established treatment for inflammatory bowel disease. Unfortunately, largely due to the sulfapyridine component, up to one-third of patients experience some adverse reaction that limits its use.^{1,2} Sulfasalazine-hypersensitive patients can be successfully desensitized²⁻⁸; however, since 5-aminosalicylic acid (5-ASA) is the drug's active moiety, pure oral 5-ASA preparations (olsalazine and mesalamine) have become widely used alternatives. Infrequently, hypersensitivity to 5-ASA itself develops,³ thus dramatically limiting a patient's treatment options. The feasibility of oral desensitization to 5-ASA has been the subject of controversy. We report three successful oral desensitizations in two patients.

CASE REPORTS

Our first case was a 75-year-old woman with a 7-year history of ulcer-

ative colitis. After initial intolerance to sulfasalazine, she had done well with up to 2.5 g of daily oral 5-ASA (olsalazine, Dipentum) for 6 years before developing a rash. This generalized, maculopapular rash persisted for 2 weeks; then resolved within 4 days of stopping her olsalazine. Off olsalazine, her colitis worsened and required hospitalization for pain control, hydration, and corticosteroids. Offered a colectomy, she chose to resume olsalazine. With the protocol on Table 1, she again tolerated a 2-g dose of 5-ASA without rash. However, one month after tolerating desensitization, she failed to improve significantly and chose a colectomy.

Case two, a 15-year-old female with Crohn's disease needed desensitization to oral 5-ASA twice. She had had generalized urticaria and angioedema after using mesalamine (Asacol). Upon stopping mesalamine, her rash resolved within a week. Using the same protocol as in case one, she again tolerated the same dose of mesalamine without hives or angioedema. At the time of a surgical procedure, her mesalamine was stopped and she continued to do well; however 2 years later her Crohn's disease recrudesced. We implemented the same protocol and she again proved tolerant of therapeutic dosage.

Despite extensive evaluations, alternative causes for the cutaneous reactions could not be found in either case. There was no evidence of food, viral, or other systemic triggers. Other medications were much less suspect and either the eruptions resolved despite their continuation or failed to recur when the medications were restarted after the desensitization protocol. Corticosteroid bursts for colitis flares were used during two of the three desensitizations.

METHODS

With informed consent, we used the regimen in Table 1 for desensitization. The pharmacy crushed 250 mg mesalamine (Pentasa) capsules. Each 2.15 mg of ground powder contained 1 mg of 5-ASA. After weighing, we administered the doses as shown in Table 1.

RESULTS

These two patients had rashes typical of 5-ASA reactions and no other explanation could be found. In each case, stopping the drug resulted in remission of the eruptions. During the course of desensitization, neither patient developed a rash, neither a maculopapular rash for patient 1 nor an urticarial rash per patient 2. Furthermore, after desensitization, each patient tolerated a dosage that caused the previous eruption.

DISCUSSION

Our observations show that successful desensitization with oral 5-ASA is possible. The term "graded-challenge" may be more appropriate in these cases that lack confirming rechallenge reactions and a clear underlying IgE-mediated mechanism. Drug rechallenge was unadvisable in our patients and although excipients are extremely unlikely causes of reactions, Pentasa was used in place of Dipentum or Asacol.

From the Walter Reed Army Medical Center; Department of Allergy & Immunology, MCHC-AL; Washington, DC.

* Corresponding author

The views expressed in this article are those of the authors and do not reflect the official policy of the Department of Defense or other Departments of the US Government.

Received for publication November 13, 1998.

Accepted for publication in revised form March 29, 1999.

Table 1. Oral 5-ASA
Desensitization Schedule

Dose	Time	Milligrams
1 (Day 1)	0:00	.025 (powder)
2	0:20	.05
3	0:40	.10
4	1:00	.18
5	1:20	.37
6	1:40	.75
7	2:00	1.5
8	2:20	3.0
9	2:40	6.0
10	3:00	12.5
11	3:20	25
12	3:40	50
13	4:00	100
14	4:20	200
Day 2-6	AM	250 (tablet)
Day 7-11	AM	250
	PM	250
Day 12-15	AM	500
	PM	250
Day 16-20	AM	500
	PM	500
Day 21+	Continue to increase as needed	

Others have contended that oral 5-ASA desensitization is not possible.^{8,9} One published protocol has called for 3 weeks of daily 5-ASA

enemas, before any oral dosing.⁹ The authors reasoned that 5-ASA must come into contact with the inflamed bowel wall for desensitization to occur. When we crushed 5-ASA, however, it would have lost its delayed-release properties and been almost entirely absorbed in the upper gastrointestinal tract. For this reason, we infer that systemic absorption via the oral route may actually favor desensitization, rather than hinder it. Regardless, the oral route clearly does work. Further, we speculate that given a choice, at least a few patients would prefer desensitization orally rather than rectally.

REFERENCES

1. Das KM, Eastwood MA, McManus JPA, Sircus W. Adverse reactions during salicylazosulfapyridine therapy and the reaction with drug metabolism and acetylator phenotype. *N Engl J Med* 1973;289:491-495.
2. Taffett SL, Das KM. Desensitization of patients with inflammatory bowel disease to sulfasalazine. *Am J Med* 1982;73:520-524.
3. Fardy JM, Lloyd DA, Reynolds RPE. Adverse effects with oral 5-aminosal-

icylic acid. *J Clin Gastroenterol* 1988; 10:635-637.

4. Bax DE, Amos RS. Sulphasalazine in rheumatoid arthritis: desensitising the patient with a skin rash. *Ann Rheum Dis* 1986;45:139-140.
5. Koski JM. Desensitization to sulphasalazine in patients with arthritis. *Clin Exp Rheumatol* 1993;11: 169-170.
6. Purdy BH, Philips DM, Summers RW. Desensitization for sulfasalazine skin rash. *Ann Intern Med* 1984;100: 512-514.
7. Holdsworth CD. Sulfasalazine desensitisation. *Br Med J* 1981;282:110.
8. Tolia V. Sulfasalazine desensitization in children and adolescents with chronic inflammatory bowel disease. *Am J Gastroenterol* 1992;87: 1029-1032.
9. Smart BA, Adams CA, Lewis ST, Altman LC. Mesalamine desensitization for a patient with ulcerative colitis. *J Allergy Clin Immunol* 1998;101:S141.

Correspondence should be addressed to:

MAJ Robert C. Stelzle, MD
Walter Reed Army Medical Center
Department of Allergy & Immunology
Building 2, Suite 1J, 1625 16th Street, NW
Washington, DC 20307-5001