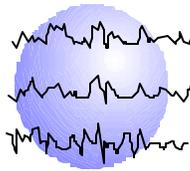


DO ALLERGIC REACTIONS TO SULFONAMIDE ANTIBIOTICS PREDICT ALLERGY TO ZONISAMIDE?

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ABSTRACT

RATIONALE:

The package insert for Zonegran[®] (ZNS) states, “Zonegran is contraindicated in patients who have demonstrated hypersensitivity to sulfonamides or zonisamide.” However, no direct evidence is available to support this statement. Because ZNS is structurally stereospecifically different from sulfonamide antibiotics, the cross-reactivity is not known. The objective of this report is to review our experience with patients who have a history of hypersensitivity to sulfonamides and were treated with ZNS.

METHODS:

All patients seen at the Minnesota Epilepsy Group are asked to report any allergies. The type of allergic action is then clarified (e.g., rash, urticaria, angioedema, etc). Fifteen adults and children who reported “sulfa” allergy as a rash, had also been treated with ZNS. The allergic reaction to the sulfonamide antibiotic was investigated through review of medical records and patient contact for validation. Charts were reviewed for cross-hypersensitivity reactions.

RESULTS:

Despite the report of rash caused by sulfonamide antibiotics in all 15 patients, in only 8 could we find good supportive evidence to validate this reaction. There were 4 males, 4 females ages 9 to 78 years old. Median age was 25 years. No rash or allergic reaction of any type occurred in these 8 patients. Seven patients continued treatment with ZNS with benefit. One discontinued after 3 months due to lack of improvement in seizure control. No hypersensitivity reaction to ZNS was seen in any of the 15 patients reporting rash.

CONCLUSION:

These numbers are small, but the stereospecific structure of ZNS is different from that of sulfonamide antibiotics. This may decrease hypersensitivity and cross-reaction significantly. Patients with intractable epilepsy and a history of rash from “sulfa” drugs may benefit from a cautious trial of ZNS.

INTRODUCTION

Many medications contain sulfur, and sulfur-containing drugs with an SO_2NH_2 moiety are known as sulfonamides. Sulfonamides can be divided into 2 large groups (see Figure):

1. Arylamines – the group containing antibiotics
2. Non-arylamines – the group containing almost all other sulfonamides (e.g., diuretics, sulfonyleureas, some nonsteroidal anti-inflammatory drugs, sumatriptan, and the antiepileptic medication zonisamide)

Sulfonamide antibiotics (also known as “sulfa” drugs) more commonly produce allergic reactions. However, an allergic reaction to sulfonamide antibiotics has not been proven to predict cross-hypersensitivity to other sulfonamide drugs.

Zonisamide (Zonegran[®], ZNS) is a novel sulfonamide anticonvulsant that has been available in Japan for more than a decade and was approved by the United States Food and Drug Administration in 2000 for the treatment of partial seizures in adults. ZNS has multiple mechanisms of action and a broad spectrum of activity across various seizure types. ZNS is contraindicated in patients with hypersensitivity to sulfonamide drugs¹; however, the cross-hypersensitivity between ZNS and sulfonamide antibiotics is currently unknown. The objective of this report is to review experience with patients who have a history of hypersensitivity to sulfonamides and were treated with ZNS.

METHODS

All patients seen at the Minnesota Epilepsy Group are asked to report any allergies. The type of allergic action is then clarified (e.g., rash, urticaria, or angioedema). Fifteen adults and children who reported a sulfa allergy as a rash had also been treated with ZNS. The allergic reaction to sulfonamide antibiotics was investigated through review of medical records and patient contact for validation. Charts were reviewed for cross-hypersensitivity reactions.

RESULTS

- 15 patients reported rash caused by an allergic reaction to sulfonamide antibiotics and were treated with ZNS.
 - Overall, 4 patients were male and 11 were female. Median age was 28 years (range=9 to 78 years).
 - 8 patients (53.3%) had supportive evidence in their medical records to validate the report of an allergic reaction.
 - Of these patients, 4 were males and 4 were females. Median age was 25 years (range=9 to 78 years).
- None of the 15 patients had any type of rash or allergic/hypersensitivity reaction to ZNS.
- All 8 patients with substantiated hypersensitivity to sulfonamides had at least a 3-month trial of ZNS (mean=12.7 months, range=3 to 26 months).

- Of these 8 patients, 7 continued on ZNS with benefit.
- 1 patient discontinued ZNS after 3 months due to a lack of improvement in seizure control.
- Among the 7 patients who did not have substantiated hypersensitivity to sulfonamides, duration of ZNS use ranged from 2 to 29 months.
 - 1 patient discontinued ZNS due to lack of benefit.
 - 1 patient was lost to follow-up.
 - 5 patients continued ZNS treatment.

DISCUSSION

Medications labeled as sulfonamides have diverse chemical structures with one common component, an SO_2NH_2 moiety. This common component does not automatically confer cross-reactivity for allergic reactions to other sulfonamides. In particular, cross-hypersensitivity may not occur between drugs from the 2 major sulfonamide groups (i.e., arylamines and non-arylamines). The arylamine sulfonamides have features in common (e.g., an N4 aromatic amine and N1 substituent) that are absent in other sulfonamides and are thought to be key factors in adverse reactions to sulfonamides.²

No data currently support cross-reactivity of sulfonamide antimicrobial agents and other sulfonamide drugs, such as ZNS. Clinicians should be cautious about putting patients at risk for adverse side effects of medications, but such concerns should be based on data. Equal caution should be taken with regard to denying patients the opportunity for better seizure control.

CONCLUSIONS

Although this study only included a small number of patients, its results suggest that patients who are allergic to sulfonamide antibiotics do not necessarily exhibit hypersensitivity to ZNS. The structure of ZNS is different from that of sulfonamide antibiotics, which may significantly decrease cross-hypersensitivity reactions. Patients with intractable epilepsy and a history of rash from sulfa drugs may benefit from a cautious trial of ZNS.

REFERENCES

1. Zonegran [package insert]. South San Francisco, Calif: Elan Pharmaceuticals, Inc; 2001.
2. Knowles S, Shapiro L, Shear NH. Should celecoxib be contraindicated in patients who are allergic to sulfonamides? Revisiting the meaning of “sulfa” allergy. *Drug Safety*. 2001;24:239-247.

Figure

Commonly Available Sulfur-containing Drugs

