

Treatment of Refractory Chronic Daily Headache with Zonisamide: a Case Series

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ABSTRACT

Objective:

Zonisamide (Zonegran™, ZNS) is a novel anticonvulsant, with a broad mechanistic profile, including sodium and calcium channel blocking activities. This study was designed to assess the effectiveness of the use of ZNS in the treatment of refractory chronic daily headache (CDH).

Materials and Methods:

This study included 16 patients who received ZNS for prophylaxis of CDH (ie, >15 headache days/month) for at least 3 months. All patients had previously failed at least 2 prophylactic medications (mean=5.9, range=2 to 10). Patients were initiated on 100 mg/d of ZNS, and 6 were titrated to a dosage of 200 mg/d after 2 weeks. Patients kept headache diaries, which included headache frequency, duration, severity, and disability ratings. Headache severity and disability were rated using a 4-point scale (0=none; 1=mild; 2=moderate; 3=severe). Using headache diaries and clinic records, mean headache duration, frequency, severity, and disability were determined for each patient 1 month prior to initiation of ZNS therapy and again 3 months after establishment of a stable ZNS dosage.

Results:

All 16 patients were female (mean age=37.3, range=20 to 57). Prior to initiation of ZNS, patients experienced a mean of 22 headache days/month, and average headache duration was 8.46 hours. After 3 months of ZNS treatment (mean dosage=137.5 mg/d), the mean number of headache days/month was reduced by 34% to 14.5 days, and the average headache duration was reduced by 24% to 6.41 hours. Total headache time was reduced by 50% (from 186 hours/month to 93 hours/month). Mean headache rating decreased by 23% (from 1.84 to 1.41), and mean disability rating decreased by 24% (from 1.48 to 1.12).

Reports of adverse events included mild diarrhea in 2 patients and weight loss in 9 patients (mean=11 lb).

Conclusions:

The results of this study suggest that ZNS is clinically useful in patients with CDH who have been refractory to numerous prophylactic medications. Notably, total headache time was reduced by 50%, and ZNS treatment was well tolerated. Controlled trials to investigate the use of ZNS in CDH prophylaxis are warranted.

INTRODUCTION

Zonisamide (Zonegran™) is a sulfonamide anticonvulsant drug that was approved in the United States in March of 2000 and has been available in Japan since 1989. Zonisamide's mechanisms of action include blockage of sodium and T-type calcium channels. Recently, interest in the use of zonisamide in the treatment of headache has increased. This study was designed to assess the effectiveness of the use of zonisamide in the treatment of refractory chronic daily headache (CDH).

MATERIALS AND METHODS

Sixteen patients who received zonisamide for prophylaxis of CDH (ie, >15 headache days/month) for at least 3 months were included in this study. All patients had previously failed treatment with at least 2 prophylactic medications (mean=5.9, range=2 to 10). Zonisamide therapy was initiated at 100 mg/d, and 6 patients were titrated to a zonisamide dosage of 200 mg/d after 2 weeks. Patient headache diaries were used to record information regarding headache frequency, duration, severity, and disability ratings. Headache severity and disability were rated using a 4-point scale (0=none; 1=mild; 2=moderate; 3=severe). Headache diaries and clinic records were used to determine mean headache duration, frequency, severity,

and disability for each patient 1 month prior to initiation of zonisamide therapy (baseline) and again 3 months after stable zonisamide dosage was established.

RESULTS

All patients (n=16) were female (mean age=37.3 years, range=20 to 57). Prior to initiation of zonisamide therapy, patients experienced a mean of 22 headache days/month, and mean headache duration was 8.46 hours. After 3 months of zonisamide treatment (mean dosage=137.5 mg/d), the mean number of headache days/month was reduced by 34% to 14.5 days, and the mean headache duration was reduced by 24% to 6.41 hours (Table 1). Total headache time was reduced by 50% (186 hours/month at baseline, 93 hours/month on zonisamide) (Figure 1). Mean headache rating decreased by 23% (1.84 at baseline, 1.41 on zonisamide), and mean

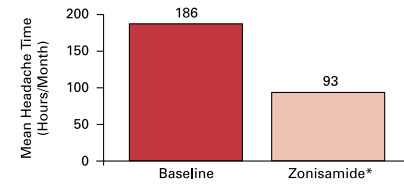
Table 1. Patient Headache Characteristics

	Baseline	Zonisamide*
Mean number of headache days per month	22	14.5
Mean headache duration (hours)	8.46	6.41
Mean headache severity rating	1.84	1.41
Mean disability rating	1.48	1.12

*After 3 months of zonisamide therapy at a stable dosage, mean dosage=137.5 mg/d

disability rating decreased by 24% (1.48 at baseline, 1.12 on zonisamide) (Table 1). Reports of adverse events included mild diarrhea in 2 patients and weight loss in 9 patients (mean=11 lb).

Figure 1. Mean Headache Time Per Month



*After 3 months of zonisamide therapy at a stable dosage, mean dosage=137.5 mg/d

CONCLUSIONS

This study suggests that zonisamide has clinical utility in patients with CDH who have been refractory to numerous prophylactic medications. Notably, total headache time was reduced by 50% after 3 months of therapy at a stable zonisamide dosage. Zonisamide treatment was well tolerated by patients in this study. Controlled trials to further investigate the efficacy of zonisamide in the prophylaxis of CDH are warranted.

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