J Headache Pain (2005) 6:77–80
DOI 10.1007/s10194-005-0155-4

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Topiramate in the treatment of refractory chronic daily headache. An open trial

Received: 18 October 2004
Accepted in revised form: 11 January 2005
Published online: 8 April 2005

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Abstract Chronic daily headache (CDH) is a debilitating disorder that becomes a treatment challenge in patients refractory to the treatment. We hereby report our experience with topiramate treatment in patients with refractory CDH. The study design was a prospective, protocol-based follow-up and retrospective analysis of headache diaries. We treated with topiramate at slowly increased moderate increments 11 CDH patients who were refractory to multiple previous treatments. Topiramate treatment was effective in 7 patients (64%). The treatment resulted in a 66% (median) decrease of the headache days per week and a significant decrease in headache severity, a reduction of the headache hours per day, and weekly analgesic consumption. These effects continued for an average follow-up of 8±4 months. The average effective dose was 100 mg/day. Slowly increasing the drug at moderate increments resulted in high tolerability of topiramate. We found topiramate to be an effective long-standing treatment option for patients with refractory CDH. Slow increments of the dosage contributed to high tolerability of the drug.

Key words Topiramate • Chronic daily headache • Headache prevention

Introduction

Chronic daily headache (CDH), defined as 15 or more headache days per month [1], may severely affect the quality of life of the patients, impairing their work and non-work activities and reducing their productivity [2]. Among these patients, those who are refractory to treatment are left with a debilitating headache disorder and constitute the most challenging population in a headache clinic.

Antiepileptic drugs play an important role in the treatment of headache disorders [3] and other pain syndromes [4–6]. Topiramate, a new generation broad-spectrum anticonvulsant, has recently been tried as a preventive drug in the treatment of various headache syndromes. These studies show that topiramate may have a place in the prevention of migraine [7–10], transformed migraine [7] and cluster headache [7, 11].

We hereby report on our experience with topiramate, shown to have possible significant adverse events (e.g., somnolence, paraesthesias and cognitive deficits), in the treatment of patients with CDH who were refractory to multiple previous treatments.

Methods

We included patients with CDH who were refractory to treatment trials with multiple modalities such as valproic acid, tri-

cyclic antidepressants, serotonin specific reuptake inhibitors, non-steroidal anti-inflammatory drugs, analgesics, greater occipital nerve blocks and acupuncture, homeopathic or herbal treatments (used by some of the patients). We included males or females older than 18 years in whom the CDH was not due to medication overuse. The patients had an ophthalmological examination prior to the treatment and their weight was monitored. Data was collected through daily headache diaries. To improve tolerability, we started topiramate at a daily dose of 12.5 mg and increased the dosage biweekly by 12.5 mg, given bid. Weekly increments were further used if no adverse events were noted.

The Institutional Review Board approved the study according to the Helsinki rules and informed consent was obtained from each subject.

Results

Eleven patients with refractory CDH were treated with topiramate. The average age of the patients was 51±13 years (64% women). The median duration of the CDH at the time of the study entry was 5 years (range 2–25 years). Five patients had CDH of transformed migraine type. The rest had CDH of tension-type headache; among them one patient had recurrent surgeries for CSF shunting (initially performed for the treatment of hydrocephalus) and 2 patients had headache related to a post-traumatic stress disorder (Table 1).

Topiramate successfully relieved headaches in 7 patients (64%). The number of headache days per week decreased by 66% (median; range 0%–96%); the headache hours per day were reduced by 50% (median; range 0–90%) and the severity of the headache lessened by 50% (median; range 0%–79%). In the 7 responders to topiramate the weekly analgesic consumption decreased by 74%±22% (average, range 50%–100%) (Table 2). These effects continued for an average follow-up of 8±4 months (range 5–14 months).

Initial headache relief was noted after 5±4 weeks of treatment. The maximal daily dose of topiramate used by the patients who had headache relief was 100 mg (median; range 25–250 mg) (Table 2). The 4 patients with no headache relief discontinued the treatment due to adverse effects (patients 10, 11; Table 2) or due to lack of efficacy (2 patients). The analgesic consumption of these patients did not change during the study follow-up.

Mild and tolerable adverse events of topiramate were reported by 7 patients (64%) and consisted of tiredness (2 patients), acral paraesthesias (2 patients) and difficulty in concentrating (2 patients) (Table 2). Weight loss and weight gain (3 kg) were noted in 2 patients.

Discussion

In this study we found that topiramate was an effective treatment for patients with refractory CDH. Of theses patients, considered as ‘treatment unresponsive’, 7 patients (64%) gained with topiramate a significant reduction in the headache frequency, severity and analgesic consumption.

Patients with CDH do respond somewhat to various medical treatments and therefore the available population was limited, but represented the most challenging population in a headache clinic. Although this was an open

Table 1 Demographic data and CDH characteristics

Patient no.	Gender	Age, years	CDH type	CDH duration, years
1	F	55	Tr. Mig.	2
2	F	63	Tr. Mig.	6
3	F	57	Tr. Mig.	2
4	M	23	TTH*	4
5	F	54	Tr. Mig.	5
6	F	69	TTH	15
7	M	49	TTH*	10
8	F	46	TTH	5
9	F	49	Tr. Mig.	4
10	M	58	TTH	25
11	M	34	TTH**	10

Tr. Mig., transformed migraine; *TTH*, tension-type headache
*Patient diagnosed with post-traumatic stress disorder
**Patient had shunt insertion for the treatment of hydrocephalus

Table 2 Results of topiramate treatment in patients with refractory CDH

Patient no.	CDH type	Time to effect, weeks	Follow-up, months	Maximal dose, given bid, mg/day	Decrease in headache days, %	Decrease in headache hours/day, %	Decrease in headache severity, %	Decrease in analgesics consumption, %	Adverse effects
1	Tr. Mig.	5	13.5	100	79	50	79	50	
2	Tr. Mig.	1	5.5	25	96	0	0	96	Unpleasant feeling
3	Tr. Mig.	8	9	75	66	90	50	90	
4	TTH*	3	12	75	75	0	75	75	
5	Tr. Mig.	4	5	125	17	54	0	50	
6	TTH	4	5	150	0	50	0	55	Diff. word finding, tiredness
7	TTH*	13	6	250	0	0	60	100	Acral paraest.
8	TTH	None	2.5	137.5					Acral paraest., diff. concentrating
9	Tr. Mig.	None	5	200					Irritability, diffic. concentrating, tiredness
10	TTH	None	1	100					Headache increase
11	TTH**	None	1	50					Dizziness, instability

Tr. Mig., transformed migraine; *TTH*, tension-type headache
*Patient diagnosed with post-traumatic stress disorder
**Patient had shunt insertion

uncontrolled study of a small population, the effect of the treatment that continued for 8±4 months is much longer than that expected for placebo. We therefore assume that it represents, in these particular our patients, a true effect of the treatment. Our results are in accordance with early observations on the usefulness of topiramate in transformed migraine [7] and we show here that the drug may be effectively used for other types of CDH.

We increased the dose of topiramate gradually in small increments. Although there were some adverse events, we assume that this modality of drug augmentation enabled the high tolerability of topiramate during the long follow-up.

Conclusions

We found topiramate to be an effective, long-lasting preventive treatment option for patients with refractory CDH. Small increments of the dosage over many weeks contributed to high tolerability of the drug.

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