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Carbamazepine in Restless Legs

A Controlled Pilot Study

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Summary. Carbamazepine or placebo were given in random order, during two four-week periods, in a double-blind, cross-over trial in six patients presenting with symptoms of restless legs. On global evaluation after completing the trial three patients and the physician preferred to continue treatment with carbamazepine. In the remaining three cases both the physician and the patients preferred not to continue with either of the treatments. However, the patients who did not give any preference also had less pronounced symptoms during treatment with carbamazepine. No patient felt better during treatment with placebo as compared to carbamazepine. The results indicate that certain patients have fewer attacks of restless legs during treatment with carbamazepine.

Key words: restless legs, carbamazepine; placebo, controlled trial, side effects

The aetiology of restless legs (Ekbom's syndrome) is unknown. Various treatments have given only partial relief, except in iron deficiency where restless legs may be cured by iron medication.

In case reports some effect of benzodiazepines and hydantoins has been claimed. As these antiepileptics had given partial relief, and as the sensation of restless legs might be due to lowered excitation threshold at rest, a controlled trial with carbamazepine was performed. The intention was to treat 20 patients, but due to lack of suitable cases only 6 patients fulfilling the inclusion criteria were treated.

Materials and Methods

Study Population

Four male and two female patients were included. Their mean age was 53 years (range 37–71 years). One patient (responder) had sensations in the surface layer of the skin, and the others had deep sensations, mostly in the calves, and also in the arms in two patients. The sensations occurred at bedtime or during the night, and two patients also had sensations of restless legs during the day.

Methods

All patients were treated as outpatients in a double-blind, cross-over fashion, with carbamazepine (Tegretol®, CIBA-GEIGY) and placebo in random order, each for 28 days. Before inclusion in the trial all patients were verbally informed of the trial methodology, that they would get two types of tablets, only one of which was expected to give relief. They were also informed that they were free to withdraw from the trial whenever they wanted. During the first treatment week in both periods the patients were given 1 tablet of carbamazepine 200 mg or placebo in the evening. If the symptoms were not sufficiently relieved the dose was increased by 1 tablet every week until a maximum dose of 1 tablet in the morning and 2 in the evening was reached. The maximum dose was reached by all six patients. Drugs affecting peripheral blood vessels and muscle relaxants were not allowed during the trial.

The number of attacks of restless leg symptoms and their severity (on a four-point scale of 0–3) was recorded every day by the patient on a follow-up chart, which was presented at the weekly visits. On the last follow-up chart the patients also blindly marked if they preferred to continue treatment with the treatment given during Period 1 or 2, or neither of them. This global subjective judgement, together with the investigators' blind global subjective judgement of treatment response, was the basis for dividing the patients into responders and non-responders.

The patients were asked to inform the investigator if they had any gastrointestinal or CNS symptoms, itching or skin disorders during the trial periods.

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Table 1. Number of days with sensations of restless legs in treatment-responders and nonresponders during administration of carbamazepine (CBZ) or placebo (P)

Treatment	Carbamazepine				Placebo				First treatment
Week	1	2	3	4	1	2	3	4	
Patient									
Responders									
ET	7	7	5	2	6	7	6	7	CBZ
RF	4	3	2	1	6	3	3	6	P
HS	3	3	3	3	5	5	4	4	P
Total	14	13	10	5	17	15	13	17	
Nonresponders									
AMN	4	6	3	4	7	3	7	–	CBZ
KGG	7	6	6	7	7	7	7	7	CBZ
AD	7	7	7	7	7	7	7	–	P
Total	18	19	16	18	21	17	21		

Table 2. Sum of severity ratings per week in responders and nonresponders during treatment with carbamazepine (CBZ) or placebo (P)

Treatment	Carbamazepine				Placebo				First treatment
Week	1	2	3	4	1	2	3	4	
Patient									
Responders									
ET	11	13	9	2	9	16	13	15	CBZ
RF	4	4	2	1	8	3	5	10	P
HS	3	3	3	3	8	6	5	4	P
Total	18	20	14	6	25	25	23	29	
Nonresponders									
AMN	6	14	5	8	17	3	16	–	CBZ
KGG	8	15	8	12	11	10	15	13	CBZ
AD	17	13	13	15	18	19	19	–	P
Total	31	42	26	35	46	32	50		
Mean severity		11.2				14.1			

Results

Six patients fulfilled the inclusion criteria and were treated with both carbamazepine and placebo in random order. Two patients were treated with placebo for only three weeks, because they wished to change the medication or they withdrew due to lack of effect on the symptoms of restless legs. In the global evaluation of the treatment three patients and the investigator wished to continue treatment with carbamazepine after the trial. Three patients and the investigator did not consider it worthwhile continuing with either preparation.

The number of days with restless leg sensations during the treatment periods is shown in Table 1. In the three responders severity of the restless leg symptoms during carbamazepine was only 21% of the corresponding value after four weeks of placebo treatment (Table 2). In nonresponders the mean severity during carbamazepine was 11.2 points, compared with 14.1 during placebo. All treated patients had lower mean scores during carbamazepine treatment than during placebo. Two patients complained of side-effects during the study; one had mild gastritis during both periods, and one had sweating, dizziness and vomiting during treatment with carbamazepine.

Discussion

The symptom of restless legs may present a serious problem in some patients. The irritating sensation may cause difficulty in concentration and severe sleep disturbances. For many years carbamazepine has been given to epileptics and it is considered to be one of the safest antiepileptic drugs. If restless legs could be relieved by treatment with carbamazepine, the therapy would be worth trying, at least in patients with advanced symptoms.

The results of the present trial confirm those presented in an earlier report [1], in which two patients treated with carbamazepine for essential tremor were also relieved of the restless leg syndrome.

The dose given here might have been too low. We have subsequently treated two patients who were relieved of their sensations after receiving carbamazepine 800 mg and 1000 mg per day, respectively. Those patients experienced a return of the sensations of restless legs after lowering the dose to 600 mg, and were again relieved by a subsequent increase in the dose.

The results of the present study and the open trial indicate that carbamazepine may relieve the sensation of restless legs at least in some patients. Further trials including larger numbers of patients and different dose regimes are needed to confirm this conclusion.

References

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