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Gabapentin in the treatment of dementia-associated nocturnal agitation

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A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
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Summary

Background: Nocturnal sleep of patients suffering from various forms of dementia is often impaired by nocturnal agitation or nocturnal wandering. Anticonvulsives such as carbamazepine or valproate are reported to have some therapeutic efficacy, but there is little information about other drugs suitable for treatment of this condition.

Case Report: Our patient, a 77-year-old Czech woman with incipient vascular dementia, received gabapentin 400mg at bedtime for 6 months and showed convincing improvement.

Conclusions: Gabapentin was very effective in treating nocturnal agitation.

key words: **gabapentin • sleep • nocturnal agitation**

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Background

Excessive motor activity during the night impairs the sleep of patients with various forms of dementia. Lack of sleep due to nocturnal agitation or nocturnal wandering is a significant burden on families of elderly demented patients and is the primary cause of institutionalization [1–4]. Nocturnal agitation may result from discomfort, pain or environmental factors; hence, identification of these potential sources is crucial. For insomnia management, eliminating alcohol and restricting caffeine intake in the early morning may help in alleviating nocturnal agitation [5]. However, if necessary, atypical neuroleptics, anticonvulsives (carbamazepine, valproate) and benzodiazepines, as well as trazodone and chloral hydrate are recommended [6]. We present the case of a patient with incipient vascular dementia accompanied by nocturnal agitation, which was successfully treated with gabapentin. To our best knowledge, no controlled study has yet been conducted to prove its efficacy in this condition [7].

Case Report

We present the case of a Czech woman, now 77 years old, who was treated for ischemic heart disease, arterial hypertension, chronic obstructive pulmonary disease and migrainous cephalalgia.

The patient was referred to our Center for Sleep Disorders for the first time in 2006 due to a history of 2 nocturnal episodes of confusion with abnormal behavior and retrograde amnesia. The patient herself could not recall these episodes, and it was not possible to retrieve further objective history. EEG showed a mild slowing of the background activity, but no epileptiform discharges were found. CT of the brain revealed dispersed postischemic changes with mild diffuse atrophy. The outcome of duplex ultrasonography of the carotid arteries was normal. As partial complex epileptic seizure was suspected, gabapentin (300 mg 3 times daily) was administered and subsequently found to have brought the patient considerable relief. Gabapentin is generally not the first-choice drug in the cases of temporal lobe epilepsy; nevertheless, we considered it appropriate because of diagnostic uncertainty and only sporadic occurrence of the episodes.

Next, the patient consulted our department in May 2008 because of 3 episodes of syncope. Cardiologic examination excluded cardiac disease as the cause, which appeared to be of cerebrovascular etiology. Since our previous diagnosis of temporal lobe epilepsy was uncertain and with respect to the 4-year seizure-free period, gabapentin was discontinued in June 2008. Two weeks after its withdrawal the nocturnal episodes of confusion with abnormal behavior reappeared. According to a room-mate, the patient was agitated in the night, shuffled about in her apartment, did not know where she was, talked aloud and was sometimes verbally aggressive. In the morning the patient could not recall the episodes, though these recurred several times during the night. These nocturnal states of confusion were the reason for her admission and video-EEG monitoring at our department.

During the monitoring, performed on 2 consecutive nights, the patient repeatedly sat up and attempted to get out of bed, but could not due to being attached to the monitor. Though confused, she reacted to the technician's statements appropriately, but with a delay. She complained of discomfort caused by the electrodes and the recurrent urge to void. The technician repeatedly told her where she was, but she continued to ask the same question.

During both nights we recorded the above-described episodes – during the first night every 20 minutes, and during the second night every 40 minutes. These awakenings occurred during superficial NREM sleep. The quality of the sleep was considerably impaired by fragmentation, by a higher percentage of stage 1NREM, and by a worse configuration of K-complexes and sleep spindles. Slow wave sleep and REM sleep were reduced. The onset and basic characteristics of REM sleep were normal. No epileptiform activity or respiratory disturbances or periodic leg movements were recorded.

During follow-up clinical examination after the video-EEG monitoring, the patient complained of memory failures for the first time, and for this reason a psychological examination was performed, which revealed low-grade organic deterioration of cognitive functions with excursive thinking, impairment of encoding and retrieval of information and normal spatial orientation. The mini-mental state examination (MMSE) score was 26 and the Cohen-Mansfield Agitation Inventory (CMAI-long form) score was 39. Thus, we suspected incipient vascular dementia.

With regard to the fact that the nocturnal episodes of confusion, sometimes accompanied by verbal aggression, were evoked by environmental influences and discomfort and by concomitant incipient vascular dementia, we concluded the case was nocturnal agitation (nocturnal wandering). We recommended elimination of the evoking factors, and following the recommended regimen with the goal of reducing the insomnia. In spite of the regimen precautions the episodes repeated several times during most nights and we decided to begin pharmacological treatment. Since gabapentin had proved effective and well-tolerated before, we prescribed it again, with very satisfactory results.

To date, the patient has been taking 400 mg of gabapentin at bedtime for 9 months, with no recurrence of her former problems despite the relatively low dosage. Thus, we consider the effectiveness of gabapentin in this condition to be clearly demonstrated.

We confirm that the patient was able to provide informed consent.

Discussion

The use of gabapentin has thus far been only sporadically reported in this condition [7–10]. The available literature mentions only anticonvulsives (eg, carbamazepine and valproate) [5]. Therefore, we should like to call attention to our satisfactory experience of gabapentin in cases like ours. In particular, we found it suitable in geriatric patients for its minimal adverse effects and absence of pharmacokinetic interactions with respect to geriatric polymorbidity. It is noted for its anti-anxiety and hypnotic effects in psychiatric patients [11,12]. Its positive effect on the structure/quality

of sleep is well-known [13]. While its mechanism of action is not yet fully understood, it would appear to be via the modulation of glutamate-mediated excitatory synaptic transmission and gamma-aminobutyric acid (GABA)-mediated inhibitory synaptic transmission [14]. Unlike carbamazepine, it does not interfere with bone metabolism, nor does it have any adverse cardiac effects. Nevertheless, there are still limited data on its efficacy, and no controlled studies have been published to date on this topic. As we mentioned above, in most of the reviewed cases gabapentin is reported to be a well-tolerated and effective treatment for dementia-associated agitation. However, several case reports in which gabapentin was used for agitation in dementia with Lewy bodies question its appropriateness for all types of dementia-related agitation [14–16]. Indeed, paradoxical gabapentin-induced exacerbation of psychosis in a patient with schizophrenia has already been described [17].

The relevant literature recommends drugs such as benzodiazepines; however, these can aggravate the cognitive deficit, a fact of importance in our patient.

Conclusions

We present the case of a patient with incipient vascular dementia accompanied by nocturnal agitation, which was successfully treated with gabapentin.

Gabapentin appears to be useful and well-tolerated in this indication.

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