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RIVERVIEW HOSPITAL

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Gabapentin for Agitation in the Elderly with Dementia

Introduction

Gabapentin is an anticonvulsant marketed in USA in 1993 and in Canada a year later. It is classified as a third generation anti-epileptic drug; others include lamotrigine and topiramate. Although gabapentin is labeled for the treatment of epilepsy, it has been used, in psychiatry as a mood stabilizer along with the second generation anticonvulsants such as carbamazepine and valproic acid. Gabapentin has also been used in managing agitation in the elderly with dementia.

Up to 90% of the elderly with dementia tend to exhibit behavioral changes as dementia progresses. Agitation is common in these patients. The term "agitation" is frequently used to describe various behavioral problems which can be disruptive or disturbing, such as frequent calling out, screaming, hitting out, kicking, spitting, stripping, pacing, wandering, resistive to care, combativeness, and sexually inappropriateness. Treating these behaviors is always a clinical challenge.

Treatment Options

Medications including antipsychotics, serotonergic antidepressants, benzodiazepines, beta-blockers and anti-epileptic drugs have been used to manage agitated behaviors in demented patients. Conventional neuroleptics such as haloperidol and loxapine have been used extensively and are often associated with side effects such as parkinsonism, akathisia and tardive dyskinesia. Atypical antipsychotics such as risperidone, olanzapine and quetiapine are favored in recent years due to better side effect profiles, however, there are conflicting results in regards to their effectiveness.

In comparison to carbamazepine and valproic acid which may potentially cause hepatic dysfunction and hematological abnormalities, gabapentin has a relatively benign side effect profile. Therefore, gabapentin has been used extensively for the treatment of agitated behavior in demented patients. This newsletter looks at studies to justify the use of gabapentin, since it has been based on the rationale that carbamazepine and valproic acid seem to have mood-stabilizing effects as well as anti-aggressive properties.

Mechanism of Action

Although gabapentin is structurally related to GABA (gama-aminobutyric acid), it does not act through GABA receptors. Gabapentin is known to have several mechanism of action, such as increasing GABA levels and decreasing the release of monoamine neurotransmittors including serotonin. Since serotonin has been shown to be involved in the modulation of mood and anxiety, it is reasonable to postulate that gabapentin may be effective via the modulation of the serotonergic system.

Studies

In a retrospective chart review study done by a group of physicians from Stanford University, twenty-four male nursing home patients who had a diagnosis of dementia were studied. Environmental factors were ruled out for their repeated disruptive, aggressive behaviors before the institution of gabapentin. The difficult to manage behaviors include; yelling, striking out, scratching, grabbing, pounding on windows and doors, spitting constantly, and making inappropriate sexual comments. Also prior to starting gabapentin, they all have failed to respond to medications including neuroleptics, valproic acid, carbamazepine, antidepressants, lithium, cholinesterase inhibitor, benzodiazepines, either monotherapy or combination. Clinical Global Improvement scale was used after at least four weeks of gabapentin treatment. The course of treatment for the patients ranged from four weeks to two years. The average daily dose of gabapentin was 1318 mg. Of the 24 patients, two had to withdraw quickly due to excessive sedation; seventeen achieved a Clinical Global Impression rating of "much improved" or "very much improved", and four were rated as "minimally improved. One patient's behavior remained unchanged.

Twelve patients with moderate to severe dementia and severe behavioral disorders were treated with open-label gabapentin (200-1,200 mg/day) for 8 weeks in a prospective case-series design. They all failed previously to respond to neuroleptics. Results of this trial demonstrated gabapentin to be well tolerated, but only modestly effective in the treatment of severe behavioral disorders in demented patients. The reason for this may be due to low dosage used in these patients who had compromised renal function and extremely severe behavioral problems. The authors suggested further trials using gabapentin in patients with different degrees of severity of behavioral problems and different levels of cognitive impairment.

In a MINIREVIEW, the authors looked at three cases involving three elderly patients treated with gabapentin for primarily their agitation. They had a diagnosis of Alzheimer's dementia, one was treated with 100 mg TID resulting in decrease in agitation and aggression and the behavioral problems were controlled for the other two patients at 600 mg per day.

Two "Letter To The Editor" reports, dated in Feb 1997 and Oct 1999, in the Journal of Clinical Psychopharmacology stated that gabapentin may be beneficial in managing agitation in demented elderly patients. One reported a 68-year-old woman with episodic agitation and violence toward staff members in a nursing home, improvement was noted when she was treated with gabapentin 300 mg BID in addition to haloperidol 2mg HS. In the other case, a 62-year-old man with dementia due to history of alcohol abuse and head injury exhibited aggressive behavior which subsequently subsided after the initiation of gabapentin.

Gabapentin Associated Mania

A retrospective chart review to identify the occurrence of worsening of manic behavior in patients treated with gabapentin was conducted. Twenty-six patients received gabapentin as monotherapy or adjunct therapy with traditional mood stabilizers for treating mania and aggression were reviewed. There were a significant number of patients showing an increase in aggressive and manic behaviors. The age range and dosage were not mentioned in this study.

Another report of hypomania induced by gabapentin was a case involving a 49-year-old man with epilepsy and mild learning disabilities who developed symptoms of hypomania on starting gabapentin.

Use of Gabapentin at RVH

Currently 63 out of 74 patients at Riverview Hospital on gabapentin are over 65 years old. Over 95% of these geriatric patients are being treated for their behavioral problems.

The dosage ranges from 200mg to 2400 mg per day. As of today, gabapentin comes in 100 mg, 300mg,400 mg capsules available in generic brand whereas the 600 mg, 800 mg strengths only available in Trade brand and their costs are as shown below:

GABAPENTIN	PMS (GENERIC) Cost per capsule	PFIZER (Brand) Cost per capsule
100 mg	$0.25	
300 mg	$0.60	
400 mg	$0.72	
600 mg	Not available	$1.74
800 mg	Not available	$2.32

Conclusion

Gabapentin appears to be a safe and well tolerated anticonvulsant to treat the behavioral complications of dementia. The data of its effectiveness is still very limited in regards to the dosage, length of therapy, comparison to other anticonvulsants. Although there are no reports to date describing the induction of mania by gabapentin in elderly patients, this possibility still needs to be considered while treating this fragile elderly population. An established serum gabapentin level would be ideal to determine a maximum effective dose in order to avoid unnecessary medication prescribed for the elderly and expense in the health care.

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