

A retrospective chart review of gabapentin for the treatment of aggressive and agitated behavior in patients with dementias.

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ABSTRACT: In a twenty-four patient case series from retrospective chart review, we examined the use of gabapentin for the treatment of aggressive and agitated behaviors in nursing home patients with a DSM-IV diagnosis of dementia. On Clinical Global Impression ratings, seventeen of twenty-two patients were much or greatly improved, four were minimally improved and only one remained unchanged. Two of the twenty-four patients discontinued use of the medication because of excessive sedation. No other significant side effects were noted in treatment lasting up to two years.

INTRODUCTION:

Aggressive, agitated and disruptive behaviors are common in patients suffering from Alzheimer's disease and other dementias in the nursing home and in the community. {1, 2} The treatment of agitated and aggressive behavior in demented patients is difficult and complex. {3, 4, 5} Although a range of medications including neuroleptics, anxiolytics, serotonergic antidepressants, beta-blockers, and anti-epileptic drugs has been studied, positive results have been limited and inconsistent. {6-15}

Three single case reports and one three-case series suggest that gabapentin, a drug marketed for its anti-epileptic properties, may be effective in treating agitation and aggression in patients with dementia. {16, 17, 18, 19} Use of the medication has been based on the rationale that certain anti-epileptic medications such as valproate appear to have anti-manic properties as well as anti-aggressive effects {20, 21}. Except for excessive sedation in some patients, gabapentin is not usually associated with significant side effects. {22, 23} Prior to initiation of a controlled study in frail, dementing patients, we felt a case series with a larger number of patients emphasizing dose-ranging and safety issues was indicated.

METHODS:

This study was an IRB-approved retrospective chart review of consecutive nursing home cases.

Subjects:

Twenty-four male nursing home patients at a large VA hospital who met the DSM-IV criteria for one of the dementias were studied. All were admitted to the nursing home units for at least several weeks, had become adjusted to the units, but had demonstrated repeated disruptive, aggressive behaviors before gabapentin therapy was instituted. Their ages ranged from 50 to 99 with a mean age of 71.25 years and a standard deviation of 10.5 years. Most had concomitant non-psychiatric medical problems that required medications but all were stable from a non-psychiatric medical standpoint. Fifteen had other psychiatric diagnoses such as psychosis and depression, which required treatment but their aggressive behavior continued after their other psychiatric syndromes were resolved. None had a chronic pain disorder. These patients exhibited difficult nursing home management problems e.g. frequent yelling, striking out, scratching, grabbing, pounding on windows and doors, spitting constantly, and making inappropriate sexual comments. Their repetitive disruptive behaviors were eroding to unit morale

and some were threats to the safety of other patients and staff. Two had attempted to choke nursing personnel.

Characteristics of the patient group are given in Table 1.

Clinical evaluations:

All diagnoses were made following a detailed, systematic assessment by an experienced geriatric treatment team according to DSM-IV criteria. Eight patients fulfilled criteria for Dementia of the Alzheimer's Type and three for Vascular Dementia. Three patients had Dementia due to Head Trauma, one had Dementia due to Parkinson's Disease, one had Dementia due to Cerebral Anoxia, and one had Dementia not otherwise specified. Seven had Dementia due to Multiple Etiologies. The patients' Mini Mental Status Examination scores ranged from 0 to 28 with a mean score of 7. {24}

Aggressive and agitated behaviors were defined as any of those behaviors listed on the Overt Aggression Scale and the Overt Agitation Severity Scale of Yudofsky and Silver as well as on the Cohen-Mansfield Agitation Inventory. {25, 26}

During the pre-gabapentin treatment phase, twenty-three patients were treated with other anti-aggressive medications, often in combination, which failed to adequately treat their aggressive behaviors. Nineteen of the patients were treated with neuroleptics including haloperidol, risperidone, olanzapine

and quetiapine. Fifteen patients were treated with other anti-epileptics: fifteen with valproic acid and seven with carbamazepine. Fourteen were treated with buspirone and twelve had received trazodone treatment. Seven patients received antidepressant therapy but these drugs were used for the treatment of depression and not, primarily, as anti-aggressive drugs: sertraline, paroxetine, nefazodone, bupropion, and nortriptyline were the antidepressant medications used. In addition, nearly every patient had received prn lorazepam treatment in the past for aggressive behavior. One patient received lithium treatment primarily for the treatment of mania. Eight patients had received cholinesterase inhibitor (donepezil) treatment primarily as an anti-dementia drug and not as an anti-aggressive drug.

Sixteen patients received more than one of the above drugs at any one time. No patient received a drug that suppresses CNS noradrenergic activity (e.g. clonidine, guanfacine) and no patient received beta-blocker treatment for aggression prior to gabapentin treatment. Of the twenty-three patients treated with other drugs prior to gabapentin therapy, all were considered treatment failures with these other medications. Ten patients did not respond to four different anti-aggression drugs, four did not respond to three different drugs, six to two different drugs, and three to one type of anti-aggression drug.

Table 2 lists the other drugs taken by the patients concomitantly with gabapentin treatment.

All patients were started on a dose of gabapentin between 100 – 300 mg per day. Patients, who were older, had multiple non-psychiatric medical illnesses, and whose aggression or agitation did not involve harming others, were started on 100 mg of gabapentin in the morning. All other patients were started on 100 mg of gabapentin three times daily. The dose of gabapentin was then titrated upward to the dose that effectively controlled the patients' agitation or aggressiveness.

For the purposes of this report, all patients were rated by clinicians using the Clinical Global Improvement (CGI) scale after at least four weeks of gabapentin treatment. The course of treatment for the patients ranged from four weeks to two years. The raters included the treating geropsychiatrist, at least two registered nurses and at least one nursing aide. The patients were rated from 1 (“very much improved”) to 7 (“very much worse”). {27, 28}

Table 2 gives the CGI scores of the patients.

RESULTS:

Gabapentin was clinically useful in many of our patients. Twenty-four patients were started on gabapentin but two were quickly withdrawn because of excessive sedation leaving twenty-two patients who completed pre-rating treatment. One patient withdrawn (age 69) became very drowsy on 100 mg daily of gabapentin; the second patient withdrawn (age 77) become drowsy on 100 mg tid and his family did not want a lower dose to be tried after he recovered. Eleven patients took gabapentin for at least four weeks; eight had taken the drug for more than three months; two patients had taken gabapentin for at least eight months; one patient has taken gabapentin for over two years.

Seventeen patients achieved a CGI rating of “much improved” or “very much improved” and four were rated as “minimally improved”. One patient’s behavior was unchanged.

See Table 2 for the CGI ratings.

The average effective daily dose of gabapentin was 1318 mg. Fourteen patients required 1200 mg or less, daily; eight patients required 1600 mg or more, daily. The highest dose given was 3600 mg per day.

Fifteen patients remained on a variety of pre-gabapentin medications, which had been felt to be helpful for the treatment of such conditions as depression, other mood instability such as mania, anxiety or psychosis; these medications had not been effective in treating the patients' aggressive and other disruptive behaviors.

Sedation was a problem for two patients; gabapentin was well tolerated by all other patients and no other serious side effects were noted. The patients experienced no vital sign changes; no patient's fall could be directly attributed to gabapentin therapy. No patient developed neurological problems due to gabapentin treatment and no patient with a pre-existing neurological disorder had a worsening of their signs or symptoms of that disorder. No hematologic, renal, hepatic or thyroid abnormalities were noted during the period of gabapentin treatment. No patient had a sudden worsening of cognition as a result of gabapentin therapy. Anecdotally, it was noted that several patients' cognition seemed to improve after their aggression and agitation decreased with gabapentin therapy.

DISCUSSION:

Our data suggest that gabapentin is effective and well tolerated for the treatment of agitated and aggressive behaviors in patients with dementia and these data support the findings in the other case reports mentioned above.

Our study is a retrospective case series. Because this was not a controlled trial, our findings are suggestive of efficacy, but require controlled clinical trials for confirmation. Questions regarding the possible predictors of efficacy need to be systematically tested in future studies. For example, are there particular behavioral problems, which respond preferentially to gabapentin? Further questions regarding continued efficacy also need to be studied. Will the improvement we saw with gabapentin treatment continue over time? Will treatment emergent adverse effects become apparent with prolonged treatment?

In conclusion, we suggest that gabapentin treatment offers promise for treatment of aggressiveness and agitation in this group of difficult and challenging patients with dementia. We are impressed with its tolerability so far. The answers to the questions posed plus other questions await further study. We propose to undertake a randomized, double blind study comparing gabapentin treatment with other anti-aggressive treatments to provide answers to some of the questions raised by this case series.

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