

Gabapentin for the treatment of behavioral and psychological symptoms of dementia*

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ABSTRACT

Objective: To examine the efficacy of gabapentin for the treatment of behavioral and psychological symptoms of dementia (BPSD). **Design:** A retrospective chart review. **Settings:** Tertiary care geriatric psychiatry inpatient unit. **Participants:** 230 patients with BPSD. **Measurements:** The socio-demographic information, type of behaviors, co-morbid psychiatric and medical diagnoses, daily doses of medications and side-effects were recorded. **Results:** Of the 230 patients, 22 were treated with gabapentin. Twenty of these patients were on a combination of gabapentin and an antipsychotic medication while two patients were treated with gabapentin monotherapy. Eighteen of the 20 patients in the combination group tolerated the treatments with little or no side effects as did the two patients in the monotherapy group. **Conclusions:** Gabapentin may be a safe option for the treatment of BPSD in combination with antipsychotic medications. Gabapentin may also be effective as monotherapy in certain patients with BPSD.

Keywords: Behavioral and Psychological Symptoms of Dementia; Neuropsychiatric Symptoms of Dementia; Anticonvulsants; Gabapentin

1. INTRODUCTION

Behavioral and psychological symptoms of dementia (BPSD) are a heterogeneous group of non-cognitive symptoms and behaviors that occur in patients with dementia [1]. BPSD does not reflect a specific diagnostic entity, but describes an important clinical dimension of

dementia which is often the triggering event for its recognition and referral to the specialist service [2]. The development of BPSD is associated with greater impairment in activities of daily living, more cognitive decline and poorer quality of life, institutionalization and is also a major risk factor for caregiver burden [3]. In this regard, BPSD are more important than the progressive cognitive deficits of the disease, and for the care of the patients with AD [3].

Treatments available for BPSD are currently not standardized and include various non-pharmacological and pharmacological approaches [3,4]. Pharmacotherapy is usually initiated when symptoms have failed to respond to non-pharmacological interventions and are not attributable to an underlying medical condition or medication effect [3,4]. A variety of medications have been used to treat BPSD, including typical and atypical antipsychotics, antidepressants, anticonvulsant mood stabilizers, cholinesterase inhibitors, benzodiazepines and other drugs [3,4].

While the benefits of antipsychotics and anticonvulsants like valproic acid and carbamazepine in the treatment of BPSD are not clear, gabapentin, another anticonvulsant may be a potential treatment for the treatment of these symptoms [3,4]. Gabapentin is structurally related to GABA and it probably acts by interfering with the calcium channels to alter transmitter release. It is commonly used as an adjunctive therapy for partial seizures. Gabapentin is eliminated unchanged renally, and its clearance is expected to parallel the age-related decrease in glomerular filtration rate. The pharmacokinetics of gabapentin, specifically the lack of both hepatic metabolism and protein binding, makes gabapentin a drug that is potentially safer than the other anticonvulsant agents for the elderly population [5].

The efficacy of gabapentin in treating behavioral symptoms of dementia has been described in several case reports and open-label trials but its effect as an adjunct to antipsychotic treatment has not been studied [6,7]. The

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purpose of this report is to consider the efficacy of gabapentin as an adjunctive therapy to antipsychotics and also as monotherapy for behavioral and psychological symptoms of dementia.

2. Methods

The data for this case series is derived from a retrospective chart review of 230 demented inpatients, discharged between July 1st, 2002 and March 31st, 2007 from the Geriatric Psychiatry Unit of a University Hospital. All these patients were diagnosed with dementia according to the Diagnostic and Statistical Manual of Mental Disorders, Text Revision, 4th edition (DSM-IV-TR) [8].

Medications given to treat these patients were evaluated and the charts of all patients who had BPSD and were treated with gabapentin were selected for this review. Patients were treated with gabapentin if they could not tolerate higher doses of the antipsychotic agents and need further stabilization of their behavioral problems. The socio-demographic information, co-morbid psychiatric and medical diagnoses, daily doses of gabapentin and antipsychotics, effects and side-effects of gabapentin were recorded.

As this was a retrospective chart review, a waiver of consent was obtained from the University Institutional Review Board for the conduct of this study.

3. Results

The total number of patients with dementia who were treated with gabapentin was twenty-two. Twenty of these patients were on a combination of atypical antipsychotic medication and gabapentin while two patients were treated with gabapentin monotherapy.

The average age of the patients in the study was 73 ± 8.69 years. There were 15 male patients with an average age of 73.78 years and 7 female patients with an average age of 76.57 years. Of these 22 patients, 16 were Caucasian (M:F, 10:6), 3 were African America (3:0) and 3 Hispanic (2:1) (**Table 1**).

All patients had a diagnosis of dementia, of these, 12 patients had Alzheimer's disease, 6 had dementia of

mixed type, 3 had vascular dementia and 1 patient had Lewy Body Dementia. Of the twenty-two patients, six had Folstein Mini Mental State Examination (MMSE) scores available [9]. The average MMSE score for these patients was 10.87 ± 6.02 . Sixteen of the patients were unable to co-operate with the MMSE because of severe impairment in cognitive functioning and agitation.

Agitation (verbal aggression) was the most common behavior noted in these patients. Combative behavior (physical aggression) was seen in 18 of the 22 patients. A combination of agitation and physical aggression was seen in 11 of the 22 patients. Paranoid thoughts (5/22, 23%) and inappropriate sexual behaviors (2/22, 9%) were less commonly noted in these patients. Confusion as a complaint was noted only in 5 of the 22 patients (23%).

A combination of gabapentin and an atypical antipsychotic medication was administered to the 20 patients. Eighteen of them tolerated this combination with no side effects. Two patients developed side-effects. One patient who was treated with 1800 mg/day of gabapentin and 20 mg/day of olanzapine became lethargic. The dose of gabapentin was reduced to 400 mg/day with a reduction in sedation. The other patient was being treated with 300 mg/day of gabapentin and 75 mg/day quetiapine. Because of sedation, the dose of gabapentin was decreased to 200 mg/day. None of the patients in the monotherapy group had any side-effects.

In the combination treatment group, 11 patients were on quetiapine, 6 were on olanzapine, 2 were on risperidone and 1 was on clozapine. Of the 22 patients, 10 were on Donepezil 5 - 10 mg/day and 1 was on memantine and 1 was on both donepezil and memantine. One of the patients was on valproic acid for seizure disorder, and 2 of them were on both valproic acid and gabapentin for agitation and behavioral problems (**Table 2**).

Behavioral issues in of all the patients resolved with these treatments. Twenty patients were discharged to skilled nursing facilities, 1 patient went to an assisted living facility and 1 patient went home. The average length of stay for these patients was 23.23 ± 5.66 days.

4. Discussion

Although some psychotropic medications have been found to be helpful in the treatment of BPSD, none of them have proven efficacy and benign side-effect profiles [3,4]. Elderly patients also have more medical co-morbidities and are taking multiple medications. This puts them at higher risk for developing medical complications and medication side-effects along with drug-drug interactions. These issues must be considered while giving a new medication to the older patient [3,4].

In this study, we used a combination of atypical anti-

Table 1. Demographic information of the patients.

Sex	Male (n = 15)	Female (n = 7)
Age (years)	73.78	76.57
Race		
African-American	3	0
Hispanic	2	1
Caucasian	10	6

Table 2. Diagnosis, comorbidities and psychotropic medications.

Age	Diagnosis	Comorbid medical illness	Comorbid psychiatric illness	Psychotropic medications (name/daily dosages)			
83	Dementia; mixed type (AD and vascular type), moderate	anemia, post CVA, CAD, chronic orthostatic hypotension, hypertension, AF, CRI	no	Gabapentin 400 mg	Memantine 20 mg		
64	Dementia; AD type, severe	DM type2, CAD, post MI, hyperlipidemia, vitamin B12 deficiency,	alcohol dependence with full remission	Gabapentin 800 mg	Donepezil 10 mg	Olanzapine 15 mg	
73	Dementia; AD type	vitamin B12 deficiency	MDD with anxiety	Gabapentin 600 mg	Donepezil 5 mg	Quetiapine 400 mg	
76	Dementia; AD type, moderate	hypertension, DM type II, CRI, BPH, gout	no	Gabapentin 800 mg	Olanzapine 15 mg		
67	Dementia; AD type	hypertension, urinary incontinence, BPH	no	Gabapentin 500 mg	Olanzapine 15 mg	Donepezil 5 mg	Memantine 15 mg
85	Dementia; AD type, severe	CRI, osteoarthritis, recurrent UTI, dejenarative joint disease, hypertension, stress urinary incontinence, chronic leg edema	no	Gabapentin 300 mg	Olanzapine 7.5 mg		
64	Dementia; AD type, severe	DM type II, seizure disorder, tinea corporis of the right buttock, anemia of chronic disease	no	Gabapentin 1200 mg	Valproic acid 1250 mg		
83	Dementia; vascular type, moderate	hypertension, CAD, CHF, anemia, NIDDM, hyperlipidemia	no	Gabapentin 100 mg	Quetiapine 150 mg	Donepezil 10 mg	Citalopram 30 mg
90	Dementia; vascular type	hypertension, glaucoma, post left CVA, post cyst removal in her breast	no	Gabapentin 200 mg	Quetiapine 100 mg	Donepezil 10 mg	
64	Dementia; vascular type, moderate	hypertension, CAD, DM, post bilateral above knee amputation, MRSA and vancomycin resistant enterococci wound infection left thigh	no	Gabapentin 400 mg	Risperidole 2.5 mg	Donepezil 5 mg	Valproic acid 1000 mg
68	Dementia; mixed type (AD and alcohol induced), severe	BPH, hypercholesterolemia	History of alcohol dependence	Gabapentin 1200 mg	Olanzapine 10 mg	Donepezil 10 mg	
78	Dementia; AD type, severe	hypertension, hyperthyroidism, NIDDM	no	Gabapentin 900 mg	Quetiapine 25 mg prn	Donepezil 10 mg	
79	Dementia; mixed type, severe	chronic pain, CVA, post UTI, fungal groin infection	no	Gabapentin 600 mg	Memantine 5 mg		
67	Dementia; AD type, severe	hypertension, bronchitis, GERD, hypocholesterolemia, Raynaud's disease, post lung ca, post left lung-upper lobe lobectomy	no	Gabapentin 400 mg	Clozapine 200 mg	Valproic acid 500 mg	
82	Dementia; AD type, severe	arthritis	no	Gabapentine 200 mg	Quetiapine 75 mg		
81	Dementia; AD type, severe	hypertension, BPH, history of diverticulosis	no	Gabapentin 600 mg	Quetiapine 200 mg	Donepezil 10 mg	
84	Dementia; mixed type (AD and Vascular)	delirium due to multiple medical causes, NIDDM, rapid AF, hypothyroidism, chronic anemia, post epidural hematoma, post left breast mastectomy	no	Gabapentin 1200 mg	Quetiapine 200 mg	Donepezil 5 mg	

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67	Dementia; Lewy body type	hyperkalemia, MRSA-positive, coccygeal decubitus, resolving, dysphagia secondary to dementia	no	Gabapentin 3000 mg	Olanzapine 20 mg	Donepezil 10 mg
83	Dementia; mixed type (AD and Vascular)	recurrent UTI, CVA with hemiplegia and aphasia, AF, cardiomegaly, degenerative joint disease	no	Gabapentin 2000 mg	Risperidone 2.5 mg	
59	Dementia; AD type, severe	hypertension	no	Gabapentin 2400 mg	Quetiapine 37.5 mg	Valproic acid 100 mg
78	Dementia; AD type	GERD, Parkinson's disease, hypertension	BAD type II, hypomanic episode	Gabapentin 1800 mg	Quetiapine 250 mg	
77	Dementia; mixed type (AD and Vascular), severe	IDDM, hypertension, GERD, phimosis & balanitis with penile discharge positive for MRSA	no	Gabapentin 200 mg	Quetiapine 400 mg	

AD = Alzheimer's Disease; CVA = Cerebral Vascular Accident; CAD = Coronary Artery Disease; CRI = Chronic Renal Failure; MI = Myocardial Infarctus; BPH = Benign Prostate Hypertrophy; UTI = Urinary Tract Infection; CHF = Chronic Heart Failure; NIDDM = Non-Insulin Dependent Diabetes Mellitus; MRSA= Methicillin Resistant *Staphylococcus aureus*; GERD = Gastroesophageal Reflux Disease; AF = Atrial Fibrillation; MDD = Major Depressive Disorder; BAD = Bipolar Affective Disorder.

psychotic medication and gabapentin, which appears to be effective and well tolerated in the treatment of BPSD. Gabapentin was also effective as monotherapy for the treatment of two cases of BPSD. Side-effect profile was relatively benign and no drug-drug interactions were noted. Our finding is in keeping with the case-series by Moretti *et al.* [6], Herrmann *et al.* [7], where they found that gabapentin monotherapy was well tolerated and effective for the treatment of BPSD. However, our study also indicated that gabapentin was well tolerated even in combination with atypical antipsychotics.

As this study is a retrospective chart review and has potential for bias, further controlled studies are necessary to confirm the efficacy of the combination treatments for BPSD. However, this current study provides the proof that elderly patients with BPSD tolerate a combination of psychotropic medications, if these medications are dosed appropriately and monitored carefully.

5. Conclusion

Behavioral and psychological symptoms are common in dementia. The treatment for these important symptoms is not standardized and is limited by the side-effect profile of the various drugs. Gabapentin, an anticonvulsant medication may be beneficial in combination with antipsychotic agents or as monotherapy for patients presenting with these behaviors.

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