Buspirone for the treatment of dementia with behavioral disturbance

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Abstract
Behavioral disturbances are common but serious symptoms in patients with dementia. Currently there are no FDA approved drugs for this purpose. There have been case reports and small case series of the use of buspirone. In this retrospective study, we review 179 patients prescribed buspirone for treatment of behavioral disturbance in dementia to better characterize the efficacy and potential side effects. All patients prescribed buspirone for behavioral disturbance due to dementia from a geropsychiatric outreach program were reviewed. Data was collected and analyzed using SPSS. One hundred-seventy-nine patients met criteria for the study with a mean age of 83.8 ± 7. Alzheimer’s dementia was the most common dementia (n=111; 62%) followed by vascular type (n=81; 45.5%). Behavioral disturbances were mainly verbal aggression (n=125; 72.3%), and physical aggression (n=116; 47.5%). Using the Clinical Global Impression scale, 72.8% of patients responded to buspirone, with 30.8% being moderately to markedly improved. The mean dose of buspirone was 25.7 mg ±12.50. Buspirone appears to be effective in treating behavioral disturbances in dementia. Future prospective and double blinded studies are needed.

INTRODUCTION
Behavioral disturbances (BD) are common in patients with dementia and increase the risk of institutionalization, caregiver burden and risk of elder abuse (Sourial et al., 2001; Cohen-Mansfield, 2008). BD also decrease the quality of life for both patient and caregiver. BD includes verbally aggressive behaviors (e.g., swearing, threats), verbally non-aggressive behaviors (e.g., repetitive vocalization, pleas for help), physically aggressive behaviors (e.g., hitting, biting, scratching, kicking, punching), and physically non-aggressive behaviors (e.g., pacing, wandering) (Sourial et al., 2001; Cohen-Mansfield, 2008).

Management of BD includes both pharmacological and non-pharmacological interventions. For patients with mild agitation, non-pharmacological interventions, such as decreasing environmental stimuli, may be effective (Sadowsky et al., 2012). However, if behaviors continue, pharmacological steps may be employed. Currently, no medication is FDA approved for the treatment of behavioral disturbances in dementia. Among psychotropic drugs, only antipsychotic agents show superiority over placebo for the treatment of psychosis and agitation-aggression in patients with dementia, although they are associated with only low to moderate efficacy. However, antipsychotics are often discontinued because of adverse effects and because federal regulations encourage early discontinuation (Devanand, 2012).

Buspirone is a 5HT1A partial receptor agonist approved in 1986 for the treatment of generalized anxiety disorder. The use of buspirone in the treatment of agitation in dementia has been described however there are no placebo controlled trials (Smith et al., 1992; Desai et al., 2012; Tariot, 1997; Cooper, 2003;
Colenda, 1998). One small blinded study compared 17 nursing home patients on buspirone (15 mg/d) with 14 patients treated with haloperidol (1.5 mg/d) for 10 weeks, and found that buspirone significantly decreased muscle tension and anxiety compared to haloperidol, and was well tolerated (Cantillon et al., 1996). Buspirone’s safety profile and low potential for dependence makes it an attractive option for the treatment of agitation in patients with dementia. We present a retrospective study of the use of buspirone for the treatment of patients with dementia and behavioral disturbances.
METHODS

A retrospective chart review of patients managed by our geriatric psychiatric outreach program to nursing home and assisted living facilities, was conducted. Inclusion criteria included patients with a diagnosis of dementia, ages 65 and over, treated with buspirone for behavioral disturbance, rather than anxiety. Of 2311 patients, 179 met inclusion criteria. Data collected included age, gender, marital status, race, type of dementia, other psychiatric diagnosis, compliance with medications, dose and length of treatment of buspirone was used, response to buspirone as assessed using the Clinical Global Impression Scale 0, (unchanged or worse) to 3 (marked or complete remission), any side effects noted, and other psychotropic medications if any. Data was entered into SPSS and the data was analyzed. The study was approved by the institutional IRB.
RESULTS

There were 60 males and 119 females, mean age 83.8 ± 7 years. The majority were widowed (n=97; 56.7%), with 49 married (28.7%), 17 single (9.9%), and 8 divorced (4.7%). Patients resided in nursing homes (n=136; 76.8%) and in assisted living facilities (n=38, 21.5%). Most patients had children (n=126; 76.4%) and had a history of employment (n=111/127; 87.4%). Mean education level was 13.0 ± 3.3 years.

Alzheimer’s disease was the most common type of dementia (n=111; 62%) followed by vascular type (n=81; 45.5%), Parkinson’s Dementia (n=7, 3.9%) alcohol related dementia (n=5, 2.8%), and frontotemporal dementia (n=3,1.2%). The majority were also diagnosed with depression (n= 129; 72.1%) with 2 diagnosed with bipolar disorder (1.1%) and 2 with schizophrenia (1.1%). Ten had co-morbid diagnoses of anxiety disorders (n=10; 5.6%). Eighteen (10.1%) had a diagnosis of alcohol abuse/dependence and one carried a personality disorder diagnosis (0.6%). Twenty-three patients (12.8%) had a history of psychiatric hospitalization and only one patient (0.6%) had a history of attempted suicide. No patients had ever received ECT.

Behavioral disturbances were mainly verbal aggression (n= 125; 72.3%), and physical aggression (n=116; 47.5%). Patient were aggressive during care (n=80, 54.1%) or were hitting without provocation (n=52; 35.1%). Pacing behavior was found in 61 out of 150 patients (40.7%). These aggressive behaviors were found to happen throughout the day in 49 out of 101(48.5%), 3 patients were
aggressive only during the morning (3%), 30 were aggressive only in the afternoon and evening (29.7%), and seven patient only at night time (6.9%). Twelve patients (11.9%) demonstrated aggression only during care.

Current use of psychotropic medications other than buspirone revealed 41 patients (23%) were taking an SSRI, 85 patients (47.5%) an SNRI, 6 patients (3.4%) were on bupropion, 1 patient (0.6%) was on a MAOI, 22 patients (12.3%) on mirtazepine, and 38 patients (21.2%) on trazodone. Seven patients (3.9%) were on a typical antipsychotic and 117 patients (65.4%) were on an atypical antipsychotic. 27 patients (15.2%) were taking benzodiazepines, and 18 patients (10.1%) were on a mood stabilizer. Only 15 patients (8.5%) were taking sleep medications.

Table 1 summarizes the changes in behavior as ranked by the Clinical Global Impression scale while the patient was on buspirone.

When buspirone was ineffective, 77 patients (66.4%) were placed on an antipsychotic, 9 patients (7.8%) tried an antidepressant (SSRI/SNRI), 2 patients (1.7%) were placed on a benzodiazepine, and 4 patients (3.4%) tried a mood stabilizer, other medications were tried in 24 patients. These medications were effective in 72 patients (71.3%) but there were 29 patients (28.7%) that did not respond to any medications.
Our study did not find gender differences related to buspirone use and treatment of aggression, including dose and effectiveness. We also did not find any correlation between age and the dose of buspirone that was effective.

The mean total dose of buspirone prescribed was 25.7 ± 12.5 mg. Buspirone was scheduled twice a day in 74 patients (41.8%) and three times a day in 95 patients (53.7%). Four patients (2.3%) received once a day and 4 patients (2.3%) four times a day. Buspirone was used for less than 4 weeks in 14 patients (8.1%), 44 patients (25.4%) used it between 1 and 6 months, and 48 patients (27.7%) between 6 and 12 months. 29 patients (16.8%) used buspirone for more than 1 year, 32 patients (18.5%) for more than 2 years, and 6 patients (3.5%) for more than 5 years. Due to positive response to buspirone, the physician was able to reduce or stop other medications on 11 patients.
DISCUSSION

Our sample of elderly dementia patients had high rates of behavioral disturbance with 72.3% verbal aggression and 47.5 % physical aggression. Other types of aggression such as throwing objects occurred in 26.7% of patients. Behaviors were common, occurring daily on average, and typically more than once per day. Our study did not find any gender differences related to the type or frequency of aggression.

The results show that 72.8% of patients responded to buspirone, with 30.8% being moderately to be markedly improved. The mean dose of buspirone was 25.7 mg ±12.50. This shows that buspirone can be effective across a wide dosage range, with even low doses being effective in some cases. In patients in which buspirone was ineffective, other drugs, such as antipsychotics and mood stabilizers, were tried. We found that about a third of these patients still exhibited behavioral disturbance, even after the use of other treatment options.

This study adds to the literature of the use and effectiveness of buspirone for agitation in elderly patients with dementia. This study has the largest sample size of dementia patients treated with buspirone for BD. Although our study has limitations due to the retrospective design and no control group, the results suggest that buspirone may be an effective and safe treatment option for patients with dementia and behavioral disturbance. Given the FDA warning for antipsychotic drugs in this population, and the potential serious side effects with other drugs such as valproic acid, buspirone is an attractive choice due to low risk of side effects. Prospective, double blind placebo controlled studies
examining the tolerability and effectiveness of buspirone in this patient population are needed to confirm these results.

Conflict of interest: None

Description of author's roles:

Maria R. Santa Cruz MD – Formulation of research question, literature review, data collection, data analysis, writing and editing of manuscript

Priscilla Hidalgo MD – Formulation of research question, data collection, data analysis, editing of manuscript

Meredith Lee DO - Formulation of research question, data collection, data analysis, editing of manuscript

Cornelius Thomas MD - Formulation of research question, literature review, editing of manuscript

Suzanne Holroyd MD – Formulation of research question, data analysis, writing and editing of manuscript

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REFERENCES


**TABLE 1 – Clinical Global Impression Scale – Behavioral Change while on buspirone**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Count (%)</th>
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<tbody>
<tr>
<td>0</td>
<td>unchanged</td>
<td>46 (27.2%)</td>
</tr>
<tr>
<td>1</td>
<td>minimal or slight improvement that doesn't alter care of patient</td>
<td>48 (28.4%)</td>
</tr>
<tr>
<td>2</td>
<td>moderate: definite improvement; partial remission of symptoms</td>
<td>47 (27.8%)</td>
</tr>
<tr>
<td>3</td>
<td>marked: complete or near complete remission</td>
<td>28 (16.6%)</td>
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