ARTICLE

Evidence-Based Pharmacological Management and Treatment of Behavioral and Psychological Symptoms of Dementia

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Behavioral and psychological symptoms of dementia (BPSD), also known as neuropsychiatric symptoms, are a heterogeneous set of symptoms and disruptive behaviors that negatively affect patient care and significantly increase the burden on caregivers and family members (1, 2). BPSD has also been used as a broad, nonspecific term encompassing symptoms and behaviors that result from complex etiopathologies related to changes found in Alzheimer's disease, vascular dementia, and other neurodegenerative disorders (1). Consequently, BPSD may present in a variety of ways, including mood symptoms, anxiety, psychotic symptoms (e.g., hallucinations and delusions), impaired sleep, aggression, and agitation (3). Unsurprisingly, BPSD has been associated with higher rates of early institutionalization and costs as a result of these problematic behaviors and psychological symptoms (4, 5).

Although nonpharmacological options, such as exercise, cognitive therapy, and caregiver education, are the preferred initial treatment modalities for BPSD among elderly adults (6), clinicians may find themselves requiring more intensive management if symptoms fail to abate. In addition, there is an impetus for providers to employ alternative treatments to manage BPSD early to improve patient care and quality of life in the long-term. Thus, the aim of the present study is to educate providers about evidence-based pharmacological treatments for BPSD to improve patient care in the geriatric population. Note that this article is not intended to be a thorough systematic review of pharmacological treatments for BPSD but rather a narrative review, with a focus on educating providers about contemporary treatment options for these increasingly prevalent neuropsychiatric symptoms.

PHARMACOLOGICAL MANAGEMENT OF BPSD

Behavioral and psychological symptoms that could affect patient safety, patient health, and patient care may not be fully treated with nonpharmacological interventions alone. Therefore, pharmacological management may become necessary to stem and alleviate symptom progression. Several meta-analyses of studies investigating pharmacological treatments for BPSD have been conducted to aid physicians in employing evidence-based medicine when treating patients with dementia. The following sections detail current evidence regarding the use of several psychopharmacological classes in treating BPSD.

Antidepressants

A meta-analysis of several studies investigating antidepressants and their effect on agitation and psychosis symptoms that present in dementia indicated a reduction of agitation symptoms when patients were prescribed sertraline and citalopram, compared with placebo (7). In addition, these reports noted that there were no significant differences in outcome measures of agitation and psychosis symptoms between selective serotonin reuptake inhibitors (SSRIs) and first- or second-generation antipsychotics, although they also noted that citalopram had a better side-effect profile, compared with perphenazine. Nevertheless, the authors reported that SSRIs and trazodone were relatively well tolerated compared with placebo. This finding was supported by Henry and colleagues (8), who reported that eight trials demonstrated the benefits of using SSRIs and trazodone in managing BPSD, which was well tolerated by patients. More specifically, they found that most studies found benefits with sertraline, trazodone, and citalopram for BPSD, mixed results with paroxetine, and failed trials with fluoxetine and fluvoxamine. However, data are still limited on the efficacy of antidepressants for the range of symptoms in BPSD other than depression, which suggests that further research is needed to determine the primary role of antidepressants in BPSD treatment (9).

Antipsychotics

A meta-analysis by Ballard and Waite (10) investigating the use of second-generation antipsychotics for aggression and psychosis in Alzheimer's disease indicated a significant improvement in aggressive symptoms when patients were prescribed risperidone and olanzapine, compared with placebo. In addition, the authors found that risperidone caused a significant decrease in psychosis symptoms, compared with placebo. Another meta-analysis by Schneider and colleagues (11) provided evidence for the efficacy of aripiprazole and risperidone in the management of BPSD. However, the same group also conducted a randomized, double-blind, placebo-controlled trial and found that adverse effects of olanzapine, quetiapine, and risperidone may offset the advantages in efficacy of these antipsychotics in treating psycho-

sis, aggression, or agitation among patients with Alzheimer's disease, because the time to discontinuation of treatment favored placebo (12). This is important to note because the Food and Drug Administration, the Canadian Health Regulatory Agency, and the European Agency for the Evaluation of Medicinal Products have issued warnings about the association between increased cerebrovascular adverse events and antipsychotics such as risperidone and olanzapine (13). Accordingly, providers should always analyze risks versus benefits when prescribing antipsychotics to elderly patients, especially because adverse effects of antipsychotics could have a negative impact on a patient's health.

Mood Stabilizers

Konovalov et al. (14) indicated that out of the seven randomized controlled trials they reviewed, only one, which used carbamazepine, demonstrated a statistically significant benefit for BPSD presentations, compared with placebo. In addition, a review of valproate for agitation in dementia reported that low-dose sodium valproate was ineffective and that high-dose divalproex sodium was associated with too many intolerable adverse effects to be effective in the target population (15). In most of the studies reviewed, adverse effects were more frequent in the drug groups, compared with placebo groups, suggesting that mood stabilizers are relatively not well tolerated by patients with BPSD.

Alzheimer's Disease Treatments

Two meta-analyses indicated some efficacy regarding the use of Alzheimer's disease medications for the improvement of BPSD. One by Trinh et al. (16) reported that cholinesterase inhibitors produced modest improvements in neuropsychiatric and functional outcomes, compared with placebo. Another meta-analysis by Maidment et al. (17) reported that use of memantine to treat BPSD yielded modest decreases in scores on the Neuropsychiatric Inventory Questionnaire and improvement of symptoms, although sedation was reported to be a major side effect.

DISCUSSION

Initially, a trial of cholinesterase inhibitors or memantine may be used to delay the progression of cognitive decline and prevent worsening cognitive dysfunction, which may exacerbate BPSD presentations. Any cholinesterase inhibitors may be used because they all have similar efficacy and tolerability profiles (16). Next, treatment of BPSD may be based on the most significant symptom clusters affecting the patient (18). For example, use of antidepressants or mood stabilizers may be more beneficial for treating mood symptoms found in BPSD, whereas psychotic and delusional symptoms may benefit more from antipsychotics. Physicians should keep in mind the tolerability and adverse effects of these medications, especially regarding the black box warnings applied to antipsychotic use by geriatric patients.

Intractable BPSD presentations may be further managed with combinations of psychotropic pharmacological classes, depending on the symptoms that persist (19). Medications that do not provide acceptable benefits or are intolerable to patients should be tapered and discontinued before another trial is started. Caution should be used for combinations of psychotropics within the same medication classes because they may increase the risk of adverse events and side effects that could lead to significantly increased morbidity and possible death.

Even when medication trials are effective in improving BPSD presentations, the risks of continuing medications (especially in the geriatric population in which polypharmacy is rampant) should be regularly evaluated. Pharmacotherapy trials should be conducted until there is 3 or 4 months of clinical stability, after which medication tapers and eventual discontinuation should be initiated (20). Sensible and prudent use of antipsychotics should be reserved for BPSD presentations that are not sufficiently managed by other treatments. Antipsychotics should be prescribed only at the lowest effective dose and should be used for the shortest possible period, with close monitoring of any adverse events.

CONCLUSIONS

BPSD symptoms are a highly prevalent set of neuropsychiatric symptoms seen among patients with neurocognitive disorders as the disease process worsens, leading to a significant burden on patients and caretakers and poorer outcomes. BPSD presentations that do not improve with only nonpharmacological approaches may require augmentation with pharmacological therapy. However, providers should always note the risks of prescribing medications for these symptoms and behaviors, because drug therapy can cause severe adverse effects that should be carefully weighed against potential benefits. Therefore, medications should be prescribed only at minimum effective doses to decrease the risk of intolerable side effects, with a plan to taper and discontinue the medications when symptoms stabilize.

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KEY POINTS/CLINICAL PEARLS

- Behavioral and psychological symptoms of dementia (BPSD) are highly prevalent neuropsychiatric symptoms that result in poorer outcomes.
- Providers should focus pharmacological therapy on the most problematic symptom clusters and use augmentation for intractable BPSD presentations only when other treatment options have been exhausted.
- Antipsychotic prescribing should be routinely evaluated because of the black box warning for the geriatric population.

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