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Our Mission: Helping to prepare Iowa’s health practitioners to care for our growing population of elders. E-NEWS is one of our methods of teaching through technology.

Each month, E-NEWS delivers abstracts from current multidisciplinary healthcare journal articles related to a specific geriatric topic. This month’s E-NEWS focuses on PHARMACOLOGIC MANAGEMENT OF NEUROPSYCHIATRIC SYMPTOMS IN DEMENTIA.

PHARMACOLOGIC MANAGEMENT OF NEUROPSYCHIATRIC SYMPTOMS IN DEMENTIA

In this issue of the E-NEWS, you will find abstracts for:

- A review that outlines the current evidence for approaches to the treatment of agitation and aggression in people with Alzheimer’s disease.
- A study that investigates relapse risk after discontinuation of risperidone in Alzheimer's disease.
- An article that discusses the management of behavioral problems in Alzheimer's disease.
- A study that evaluates the response of agitated behavior to pain management in people with dementia.
- An article that reviews the pharmacological treatment of dementia.
- A study that examines the efficacy and safety of pharmacological treatments for neuropsychiatric symptoms of dementia in long-term care.
- An article that describes a research project designed to increase appropriate antipsychotic prescribing for older adults with dementia.
- An article that addresses safety concerns in atypical antipsychotic use in people with dementia.
- A study that seeks to determine whether treatment with valproate could delay or prevent emergence of agitation or psychosis in people with Alzheimer's disease.
- An article that assesses the cognitive effects of atypical antipsychotic medications in people with Alzheimer's disease.

PURPOSE OF REVIEW: Agitation and aggression commonly arise in people with Alzheimer's disease (AD) and other dementias. They are distressing for the individual and often confer risk to them and to others, as well as raising significant clinical challenges. This review outlines the current evidence for pharmacological and nonpharmacological approaches to the treatment of agitation and aggression in these patients. RECENT FINDINGS: There is a growing body of literature supporting the use of nonpharmacological approaches as well as the treatment of pain as a first-line management strategy prior to psychopharmacotherapy. Antipsychotic medications are most commonly prescribed to address agitation and aggression. Evidence indicates this approach results in a modest but significant improvement in aggression in the short term (6-12 weeks) although the impact on other symptoms of agitation is limited. There is less positive evidence to support their use in the longer term, and prescriptions of more than 12 weeks and longer periods of prescription are associated with cumulative risk of severe adverse events, including death. Suggested pharmacological alternatives with the most promising preliminary evidence include memantine, carbamazepine, citalopram, and prazosin, but none of these agents have sufficient evidence in treating agitation and aggression to recommend use in routine clinical practice. SUMMARY: Currently, the best approach for managing these symptoms is within a framework of good practice that promotes prevention, monitoring and the use of nonpharmacological alternatives, with judicious short-term use of antipsychotics, when appropriate.


BACKGROUND: Among patients with Alzheimer’s disease who have had a response to antipsychotic medication for psychosis or agitation-agression, the risk of a recurrence of symptoms after discontinuation of the medication has not been established. METHODS: Patients with Alzheimer’s disease and psychosis or agitation-agression received open-label treatment with risperidone for 16 weeks. Those who had a response to risperidone therapy were then randomly assigned, in a double-blind fashion, to one of three regimens: continued risperidone therapy for 32 weeks (group 1), risperidone therapy for 16 weeks followed by placebo for 16 weeks (group 2), or placebo for 32 weeks (group 3). The primary outcome was the time to relapse of psychosis or agitation. RESULTS: A total of 180 patients received open-label risperidone (mean dose, 0.97 mg daily). The severity of psychosis and agitation were reduced, although there was a mild increase in extrapyramidal signs; 112 patients met the criteria for response to treatment, of whom 110 underwent randomization. In the first 16 weeks after randomization, the rate of relapse was higher in the group that received placebo than in the groups that received risperidone (60% [24 of 40 patients in group 3] vs. 33% [23 of 70 in groups 1 and 2]; P=0.004; hazard ratio with placebo, 1.94; 95% confidence interval [CI], 1.09 to 3.45; P=0.02). During the next 16 weeks, the rate of relapse was higher in the group that was switched from risperidone to placebo than in the group that continued to receive risperidone (48% [13 of 27 patients in group 2] vs. 15% [2 of 13 in group 1]; P=0.02; hazard ratio, 4.88; 95% CI, 1.08 to 21.98; P=0.02). The rates of adverse events and death after randomization did not differ significantly among the groups, although comparisons were based on small numbers of patients, especially during the final 16 weeks. CONCLUSIONS: In patients with Alzheimer's disease who had psychosis or agitation that had responded to risperidone therapy for 4 to 8 months, discontinuation of risperidone was associated with an increased risk of relapse.


Alzheimer’s disease (AD) is a complex progressive brain degenerative disorder that has effects on multiple cerebral systems. In addition to cognitive and functional decline, diverse behavioral changes manifest with increasing severity over time, presenting significant management challenges for caregivers and health care professionals. Almost all patients with AD are affected by neuropsychiatric symptoms at some point during their illness; in some cases, symptoms occur prior to diagnosis of the dementia syndrome. Further, behavioral factors have been identified, which may have their origins in particular neurobiological processes, and respond to particular management strategies. Improved clarification of causes, triggers, and presentation of neuropsychiatric symptoms will guide both research and clinical decision-making. Measurement of
neuropsychiatric symptoms in AD is most commonly by means of the Neuropsychiatric Inventory; its utility and future development are discussed, as are the limitations and difficulties encountered when quantifying behavioral responses in clinical trials. Evidence from clinical trials of both non-pharmacological and pharmacological treatments, and from neurobiological studies, provides a range of management options that can be tailored to individual needs. We suggest that non-pharmacological interventions (including psychosocial/psychological counseling, interpersonal management and environmental management) should be attempted first, followed by the least harmful medication for the shortest time possible. Pharmacological treatment options, such as antipsychotics, antidepressants, anticonvulsants, cholinesterase inhibitors and memantine, need careful consideration of the benefits and limitations of each drug class.


OBJECTIVES: Behavioral disturbances and pain are common in nursing home (NH) patients with dementia. An association between pain and increased agitation has been suggested, and recently a significant reduction of agitation has been demonstrated by pain treatment in patients with moderate to severe dementia. We now examined which specific agitated behaviors respond to individualized pain treatment. DESIGN: Cluster randomized clinical trial. SETTING: 60 clusters (i.e., clusters defined as single independent NH units) in 18 NHs within five municipalities of Western Norway. PARTICIPANTS: 352 patients with moderate to severe dementia and clinically significant behavioral disturbances. INTERVENTION: The control group received usual treatment and care. According to a predefined scheme for 8 weeks, all patients in the intervention group received individual daily pain treatment with acetaminophen, extended release morphine, buprenorphine transdermal patch, and/or pregabalin. MEASUREMENTS: Cohen-Mansfield Agitation Inventory subscales and items. RESULTS: Analyses demonstrated that Factor 3 (Verbally agitated behaviors) showed the largest significant difference (DF = 1204.0, t = -4.308, p <0.001), followed by Factor 2 (Physically non-aggressive behaviors) (DF = 1198.0, t = -2.672, p = 0.008), and Factor 1 (Aggressive behaviors) (DF = 1196.0, t = -2.093, p = 0.037) after 8 weeks, by a linear random intercept mixed model in two-way repeated-measures configuration with adjustment for heteroscedasticity. CONCLUSION: We found that verbal agitation behaviors such as complaining, negativism, repetitious sentences and questions, constant request for attention, and cursing or verbal aggression responded to pain treatment. In addition, restlessness and pacing were sensible to analgesics. Such behaviors should therefore lead to an assessment of pain, and pain treatment. Further studies comparing how pain treatment should be balanced against other strategies including psychotropic drugs are needed. Copyright © 2013 American Association for Geriatric Psychiatry.


PURPOSE OF REVIEW: In this article, we discuss new data on currently licensed drugs for dementia and novel developments in the management of neuropsychiatric symptoms in patients with dementia. RECENT FINDINGS: During the last years, a large body of evidence has been accumulated to support the use of antidementia medication in patients with severe Alzheimer's disease. Combination therapy with acetylcholinesterase inhibitors and memantine for Alzheimer's disease remains controversial, as controlled trials have yielded conflicting results. Memantine is not indicated in patients with mild Alzheimer's disease. Studies on memantine for Parkinson's disease dementia and dementia with Lewy bodies were inconclusive. In adult patients with dementia in the context of Down syndrome, memantine is not effective, and further studies on acetylcholinesterase inhibitors are warranted. There is still no treatment established for patients with vascular or frontotemporal dementia. The efficacy of antidepressants to treat depression associated with dementia is not proven. Treatment of agitation and psychosis in patients with dementia remains a challenge. SUMMARY: Recent systematic clinical reviews and new research on currently available treatment options provide valuable assistance for clinicians to deal with frequent clinical problems in the context of dementia.

BACKGROUND: Medications are frequently prescribed for neuropsychiatric symptoms (NPS) associated with dementia, although information on the efficacy and safety of medications for NPS specifically in long-term care (LTC) settings is limited. The objective of this study was to provide a current review of the efficacy and safety of pharmacological treatments for NPS in LTC. METHODS: We searched MEDLINE, EMBASE, PsychINFO, and the Cochrane Library for randomized controlled trials comparing medications with either placebo or other interventions in LTC. Study quality was described using the Cochrane collaboration risk of bias tool. The efficacy of medications was evaluated using NPS symptom rating scales. Safety was evaluated through rates of trial withdrawals, trial withdrawals due to adverse events, and mortality. RESULTS: A total of 29 studies met inclusion criteria. The most common medications evaluated in studies were atypical antipsychotics (N = 15), typical antipsychotics (N = 7), anticonvulsants (N = 4), and cholinesterase inhibitors (N = 3). Statistically significant improvements in NPS were noted in some studies evaluating risperidone, olanzapine, and single studies of aripiprazole, carbamazepine, estrogen, cyproterone, propranolol, and prazosin. Study quality was difficult to rate in many cases due to incomplete reporting of details. Some studies reported higher rates of trial withdrawals, adverse events, and mortality associated with medications. CONCLUSIONS: We conclude that there is limited evidence to support the use of some atypical antipsychotics and other medications for NPS in LTC populations. However, the generally modest efficacy and risks of adverse events highlight the need for the development of safe and effective pharmacological and non-pharmacological interventions for this population.


Many issues related to safety and quality care emerge from reports that nearly one in three nursing home residents is treated with antipsychotic medication, a rate that exceeds levels that led to nursing home reform more than 2 decades ago. Atypical antipsychotic medications have become the mainstay of treatment for behavioral problems among residents with dementia, despite federal "black box" warnings about health risks and research demonstrating their limited effectiveness. The purpose of this article is to briefly describe a dissemination research project designed to increase appropriate antipsychotic prescribing for older adults with dementia. A step-wise problem-solving algorithm designed to reduce unnecessary psychotropic medication use is described. Formative evaluation results provided by nursing home personnel are reviewed. Discussion focuses on nursing home culture as an important influence on the adoption of evidence-based practices and changes needed to promote use of behavioral interventions in dementia care and reduction of reliance on antipsychotic medications. Copyright 2013, SLACK Incorporated.


Neuropsychiatric symptoms such as agitation and delusions occur commonly in elderly patients with dementia and often cause significant distress. Data on treatment efficacy are strongest for atypical antipsychotics, but these agents must be used with great caution. Adverse effects in patients with dementia include an increased risk of mortality and cerebrovascular events, as well as metabolic effects, extrapyramidal symptoms, falls, cognitive worsening, cardiac arrhythmia, and pneumonia. Conventional antipsychotics may pose an even greater safety risk. No clear efficacy evidence exists to support the use of alternative psychotropic classes (e.g., antidepressants, anticonvulsants), although they may be safer options. An antipsychotic trial is warranted when nonpharmacological intervention is unsuccessful and neuropsychiatric symptoms or associated behaviors cause severe distress or pose a significant safety risk. Before an atypical antipsychotic is started, a comprehensive assessment should be performed to rule out medical causes of the neuropsychiatric symptoms and to ascertain whether any contributing environmental or caregiver factors are present. Risks, benefits, and alternatives should be discussed with the patient and surrogate decision maker, with an opportunity given to ask questions. Dosages should be the lowest necessary, and metabolic parameters should be regularly monitored. Face-to-face visits are important to monitor response, tolerance, and the need for continued treatment. For patients in whom neuropsychiatric symptoms have been much improved or have
been in remission for 3-6 months, a discontinuation trial should be considered. Through careful selection of appropriate patients for treatment, education of patients and caregivers, and close monitoring, safety risks can be minimized.


CONTEXT: Agitation and psychosis are common in Alzheimer disease and cause considerable morbidity. We attempted to delay or to prevent agitation and psychosis with the use of divalproex sodium (valproate).

OBJECTIVE: To determine whether treatment with valproate could delay or prevent emergence of agitation or psychosis. DESIGN, SETTING, AND PATIENTS: A multicenter, randomized, double-blind, placebo-controlled trial of flexible-dose valproate in 313 (of 513 screened) individuals with moderate Alzheimer disease who had not yet experienced agitation or psychosis. The study was conducted from November 1, 2005, through March 31, 2009, at 46 sites in the United States. INTERVENTION: Participants were randomly assigned to valproate treatment at a target dose of 10 to 12 mg per kilogram of body weight per day or identical-appearing placebo for 24 months followed by a 2-month period of single-blind placebo treatment. MAIN OUTCOME MEASURE: Time to emergence of clinically significant agitation or psychosis. RESULTS: A total of 122 participants (59 receiving valproate and 63 receiving placebo) completed 24 months of treatment while taking study medication; 42 (27 receiving valproate and 15 receiving placebo) reached 24 months having discontinued study medication; 150 reached month 26. There was no difference between groups in time to emergence of agitation or psychosis (Cox proportional hazard ratio, 0.96; P = .88). There was no difference between groups in change on any secondary outcome. The valproate group had higher rates of somnolence, gait disturbance, tremor, diarrhea, and weakness. Eighty-eight participants underwent magnetic resonance imaging scans at baseline and 12 months; the valproate group showed greater loss in hippocampal and whole-brain volume, accompanied by greater ventricular expansion (P < .001). CONCLUSION: Valproate treatment did not delay emergence of agitation or psychosis or slow cognitive or functional decline in patients with moderate Alzheimer disease and was associated with significant toxic effects.


OBJECTIVE: The impact of the atypical antipsychotics olanzapine, quetiapine, and risperidone on cognition in patients with Alzheimer's disease is unclear. The authors assessed the effects of time and treatment on neuropsychological functioning during the Clinical Antipsychotic Trials of Intervention Effectiveness-Alzheimer's Disease study (CATIE-AD). METHOD: CATIE-AD included 421 outpatients with Alzheimer's disease and psychosis or agitated/aggressive behavior who were randomly assigned to receive masked, flexible-dose olanzapine, quetiapine, risperidone, or placebo. Based on their clinicians’ judgment, patients could discontinue the originally assigned medication and receive another randomly assigned medication. Patients were followed for 36 weeks, and cognitive assessments were obtained at baseline and at 12, 24, and 36 weeks. Outcomes were compared for 357 patients for whom data were available for at least one cognitive measure at baseline and one follow-up assessment that took place after they had been on their prescribed medication or placebo for at least 2 weeks. RESULTS: Overall, patients showed steady, significant declines over time in most cognitive areas, including in scores on the Mini-Mental State Examination (MMSE; -2.4 points over 36 weeks) and the cognitive subscale of the Alzheimer's Disease Assessment Scale (-4.4 points). Cognitive function declined more in patients receiving antipsychotics than in those given placebo on multiple cognitive measures, including the MMSE, the cognitive subscale of the Brief Psychiatric Rating Scale, and a cognitive summary score summarizing change on 18 cognitive tests. CONCLUSIONS: In CATIE-AD, atypical antipsychotics were associated with worsening cognitive function at a magnitude consistent with 1 year's deterioration compared with placebo. Further cognitive impairment is an additional risk of treatment with atypical antipsychotics that should be considered when treating patients with Alzheimer's disease.
Next Month's Issue:

Advance Care Planning and Family Issues in Dementia

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