A Preliminary Study of Anticholinergic Burden and Relationship to a Quality of Life Indicator, Engagement in Activities, in Nursing Home Residents With Dementia

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Objectives: (1) To describe the anticholinergic burden experienced by nursing home residents with dementia using the Anticholinergic Cognitive Burden (ACB) Scale; and (2) to determine the association of anticholinergic burden and engagement in activity.

Design: Cross-sectional, using baseline data from an ongoing clinical trial.

Setting: Nine nursing homes in Pennsylvania.

Participants: Eighty-seven nursing home residents with dementia

Measurements: The ACB Scale was used to classify the severity of each resident's prescribed drugs' anticholinergic activity on cognition. Engagement in activity was measured by direct observation using a standard instrument.

Results: Across 775 observations, subjects were active approximately 54% of the time, doing nothing 24% of the time, and asleep over 21% of the time. Seventy-one (81.6%) subjects were prescribed at least one drug with anticholinergic properties and 32 (36.7%) were prescribed at least one drug with severe anticholinergic properties. On average, subjects had a total ACB score of 2.55 ($\pm$ 1.9). Mental status (MMSE) and dependency (PGDRS) were associated with engagement, but use of anticholinergic drugs was not.

Conclusion: Nursing home residents are prescribed many drugs with anticholinergic properties. The ACB Scale has utility as a tool to alert practitioners to high anticholinergic burden, who can then use this information when choosing between equally efficacious medications. Further study using larger samples of persons with dementia in earlier stages of the disease, and use of intense measurement designs are needed to more clearly determine the association of ACB with quality of life indicators. **(J Am Med Dir Assoc 2009; 10: 252–257)**

Keywords: Anticholinergic burden; activity; nursing home residents; dementia

Clinical problems, such as agitation, depression, incontinence, and sleep disorders, are common in nursing home residents with dementia and affect their quality of life. Many of the drugs used to manage these problems have anticholinergic properties and include antipsychotics, antidepressants, and antispasmodics. Although these drugs demonstrate varying degrees of efficacy, their anticholinergic properties have the potential to produce catastrophic side effects. There is

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mounting evidence indicating that sedation, increased cognitive and physical impairment, and faster functional decline are associated with use of drugs that carry a high anticholinergic burden (ACB) in older adults with dementia.[1–4]

In the nursing home, quality of life is arguably one of the most important treatment outcomes for residents with dementia. To that end, successful management of clinical problems often involves an appropriate balance of pharmacological and nonpharmacological interventions to minimize harm and attain positive health outcomes. Seminal work by Lawton[5] identified engagement in meaningful activities as a core dimension of quality of life in dementia. Clinical trials have demonstrated the utility and safety of physical and/or social activities for addressing a number of problems in nursing home residents: agitation,[6] depression,[7] sleep disorders,[8] and incontinence.[9] A key notion is that the ability to actively engage in activities is both a prerequisite for nonpharmacological treatment effectiveness, as well as a sensitive indicator of quality of life in residents with dementia.[10]

Ideally, pharmacological and nonpharmacological approaches should complement one another. Residents who have a high ACB, however, may be less likely to benefit, or may have a reduced benefit from activities that require active engagement because of the sedation and confusion that accompanies use of these drugs. As a result, residents may experience more rapid functional decline and further loss of quality of life. In an observational study of 209 nursing home residents, those taking antipsychotic drugs were significantly more socially withdrawn and spent less time engaged in activities than residents not taking these drugs.[11] Interestingly, the behaviors for which these drugs were prescribed demonstrated no association with indicators of poor quality of life. On the other hand, inactivity and low levels of engagement contribute substantially to social isolation and loss of physical function, and are strong markers of poor quality of life.[10]

The vulnerability of older adults to the negative effects of drugs with primary or secondary anticholinergic properties[12,13] has prompted the development of methods for measuring their central anticholinergic activity and cumulative impact on health outcomes. Serum anticholinergic activity assay (SAA) is currently the most direct method of measurement, but it reflects a transitional state outside the brain and its use is not practical in the clinical area.[14] Recently, several tools have been developed to help clinicians assess total anticholinergic burden using simple, noninvasive approaches that carry a high degree of clinical utility.[15–17] One of these tools, the Anticholinergic Cognitive Burden (ACB) Scale, was developed explicitly for categorizing drugs according to the severity of their negative cognitive effects.[17] Unlike similar tools, the ACB Scale is based on a systematic evidence review of the literature, input from an expert panel of clinicians, and a focus on central rather than peripheral anticholinergic effects. This latter characteristic makes the scale an appropriate choice for assessing anticholinergic burden as it relates to engagement in activities.

To establish its clinical applicability, more research is needed to validate the ACB Scale and to determine if ACB scores are associated with clinical outcomes related to anticholinergic burden. This preliminary study had 2 purposes: (1) to describe the anticholinergic burden experienced by nursing home residents with dementia using the ACB Scale; and (2) to determine the association of anticholinergic burden and engagement in activity, a significant indicator of quality of life.

METHODS

Study Design

This cross-sectional study used baseline data from an ongoing randomized clinical trial that is testing the efficacy of individualized recreational activity interventions for responding to the behavioral symptoms of dementia (ClinicalTrials.gov NCT00388544). The protocol was approval by the Pennsylvania State University Institutional Review Board and has a Data Safety and Monitoring Committee that oversees study safety and validity.

Participants

The study sample included nursing home residents with dementia who resided in 1 of 9 long-term care facilities located in central and northeast Pennsylvania. These sites were all community-based nursing homes: for profit (n = 4), nonprofit (n = 4), and one that changed from nonprofit to profit status during data collection. Bed size ranged from 32 to 404 with a mean of 164. Subjects were recruited through the nursing home. The nursing homes provided the investigators with contact information for the legally authorized representatives of 136 residents who met initial enrollment criteria and who agreed to be contacted by the investigators. Twenty of these individuals refused participation mainly because of the videotaping that was required in the protocol. Written consent was obtained from the legally authorized representative for 116 (85%) of responding residents and these residents underwent further screening. A recreational therapist and nurse researcher conducted the screen, which included measures of mental status using the Mini-Mental State Exam (MMSE),[18] physical function using the Psychogeriatric Dependency Rating Scale (PGDRS),[19] and a medical chart review. Eighty-seven (75%) of the consented residents met all enrollment criteria and were entered into the study. All 87 subjects completed the baseline period.

Enrollment criteria were as follows: English speaking; 65 years of age or older; diagnosis of dementia using DSM-IV criteria; an MMSE score of 8 or greater but less than 24; no new psychoactive drugs prescribed from prebaseline through final observation as verified by a weekly chart review; and presence of behavioral symptoms as reported by staff and documented in the latest Minimum Data Set (MDS). Exclusion criteria included admission to the facility within the past 2 months; delirium or a progressive, unstable medical, metabolic, or neurological illness; history of Parkinson's disease, Huntington's disease, seizure disorder, stroke, alcoholism, drug abuse, head trauma with loss of consciousness, or psychiatric illness preceding the onset of memory loss.

The 87 subjects in this study were enrolled between September 2005 and November 2007. The sample reflected demographic characteristics typical of nursing home residents[20]: they were female (77%), white (87%), and widowed (73%) with a mean age of 85.7 (± 6.3) years, a mean of 11.7 (± 2.9) years of formal education, and mean length of stay of 18.6 (± 15.1) months. As a group, they had moderate to severe cognitive impairments and moderate physical impairments as indicated by their mean scores of 14.2 (± 4.5) and 13.3 (± 7.4) on the MMSE and PGDRS, respectively.

Procedures

Subjects who met enrollment criteria were entered into a 5-day baseline period to establish their activity engagement over the daytime hours. Trained research assistants, blind to study aims, observed subjects for 20 minutes, twice per day, morning and afternoon between 9 AM and 5 PM. Measures of engagement were taken at each session. The observation periods were individualized for each subject and conducted at times when the subject was most likely to exhibit behavioral symptoms (agitation or passivity), a time when engagement would be difficult for the subject. The time for observation was selected based on staff report of high behavioral symptom time for each subject and a prebaseline observation period where subjects were observed every hour for 5 minutes (7 AM to 7 PM) using the Cohen-Mansfield Agitation Inventory[21] and the Passivity in Dementia Scale.[22] Thus, the individualized observation times were standardized such that all subjects were observed when they experienced difficulty with engagement relative to their usual pattern. Subjects' regularly scheduled medications were abstracted from their medical chart and entered into a data base by a geriatric nurse practitioner who scored the anticholinergic activity of each drug using the ACB Scale in consultation with the fifth author (M.B.), a developer of the scale and practicing geriatrician.

Measures

Anticholinergic burden was measured using the Anticholinergic Cognitive Burden Scale,[17] an expert-based practical index that classifies the severity of a drug's anticholinergic activity on cognition using a scale of 1 (mild), 2 (moderate), and 3 (severe). The scale was developed based on a review of all published studies from 1996 to 2007 that measured the anticholinergic activities of a drug and its association with cognitive function in older adults. The list of drugs reviewed was presented to an expert interdisciplinary panel that included geriatricians, geriatric pharmacists, geriatric psychiatrists, general physicians, geriatric nurses, and aging brain researchers. The panel categorized each medication into 1 of the 3 classes of mild, moderate, and severe based on the severity of its cognitive anticholinergic effects. Total ACB in this study was calculated by summing the ACB scores of all regularly scheduled drugs prescribed for the subject.

Engagement was measured by direct observation using Nolan et al's[23] molar coding scheme. The instrument has descriptors for behaviors that depict time use: asleep, doing nothing, informal activity, organized activity, eating/drinking, and treatment. For this study, informal and organized activity were collapsed into one category of "active." The categories of eating/drinking and treatment were not included in the analysis, as they were rarely observed and not conceptually related to the purpose of this study. At each observation point the research assistant selected the one behavior exhibited by the subject that was predominate over the 20-minute observation period (ie, occurred for more than 50% of the time). Scores ranged from 0 (asleep) to 2 (active). Inter-rater reliability was evaluated using 52 repeat observations. Overall agreement between the 2 raters was 96.2%. Agreement was evaluated using Cohen's kappa statistic, showing kappa = 0.94.

Analysis

Descriptive statistics consisting of means, standard deviations, and frequencies were calculated for the major study variables. Pearson's correlation coefficient was calculated as a measure of linear association between age, gender, length of stay (LOS), MMSE, PGDRS, and ACB scores. Engagement was categorized as "asleep," "doing nothing," or "active," coded as 0, 1, or 2.

Four variables representing ACB were coded: (1) ACB Total Score (for each subject, the sum of the ACB scores [1, 2, or 3] for all drugs prescribed), (2) ACB 3 Score (for each subject, the number of prescribed drugs with severe anticholinergic properties [ACB score of 3]), (3) any ACB (the group of subjects who were prescribed any drug with anticholinergic properties: ACB of 1, 2 or 3), and (4) any ACB 3 (the group of subjects who were prescribed any drug with severe anticholinergic properties: ACB score of 3). Associations between the ACB variables and engagement were evaluated using separate multinomial mixed models analyses implemented with generalized estimating equations (GEE), using SAS PROC GENMOD (SAS, Inc., Cary, NC). All models included subject as a random effect in order to account for correlation among the multiple observations of engagement for each subject. Engagement was used as the dependent variable for each analysis, with one ACB variable and age, gender, LOS, PGDRS, and MMSE as independent variables. Additional secondary analyses used the least squares mean of the engagement scores for each subject as the dependent variable. Multiple linear regression was used to evaluate the association of mean engagement with each of the ACB variables. Age, gender, LOS, PGDRS,and MMSE were included as covariates in each model.

RESULTS

Table 1 shows the results of the daytime engagement observations. We experienced missing data for 95 of the 870 observation points because of the unavailability of subjects (out of facility for family visit, medical testing, or engaged in personal care). No subject was excluded from analyses because of a large amount of missing data. Across 775 observations, subjects were active approximately 54% of the time, doing nothing 24% of the time, and asleep over 21% of the time.

Table 2 lists all drugs with anticholinergic properties taken by subjects, the severity of their anticholinergic activity (ACB score), and the number and percentage of subjects

Table 1. *Engagement Across 775 Observations*

Behavior	Frequency	Percent
Asleep	168	21.7
Doing Nothing	186	24.0
Active	421	54.3

taking each of these drugs. Overall, 71 (81.6%) subjects were prescribed at least 1 drug with anticholinergic properties, 49 (56.3%) subjects were prescribed 2 or more drugs with anticholinergic properties, and 32 (36.7%) subjects were prescribed at least 1 drug with severe properties. On average, subjects had 1.74 anticholinergic drugs prescribed and a total ACB score of 2.55 (± 1.9; range 0 to 8). The most frequently prescribed drugs were furosemide, metoprolol, and warfarin, all with mild anticholinergic properties. The most frequently prescribed drugs with severe anticholinergic properties were olanzapine, quetiapine, and paroxetine.

Mental status (MMSE) was significantly associated with mean engagement ($P = .002$ to .003). There were no significant associations between any of the ACB measures and mean engagement ($P = .302$, .126, .412, and .640 for any ACB, any ACB 3, ACB 3 score, and Total ACB score, respectively).

Mean MMSE was not different between those with any ACB drug and those with none ($P = .340$, *t* test), or between those receiving any ACB 3 drug and those who did not ($P = .877$, *t* test).

Table 2. *Anticholinergic (ACB) Score of Prescribed Drugs and Number of Subjects (%) Taking Each*

Drug	ACB Score	n(%)
Furosemide	1	29 (33.3)
Metoprolol	1	20 (22.9)
Warfarin	1	10 (11.4)
Olanzapine	3	9 (10.3)
Digoxin	1	8 (9.2)
Risperidone	1	8 (9.2)
Quetiapine	3	8 (9.2)
Atenolol	1	8 (9.2)
Paroxetine	3	6 (6.9)
Ranitidine	1	6 (6.9)
Oxybutynin	3	4 (4.6)
Isosorbide	1	4 (4.6)
Prednisone	1	4 (4.6)
Loperamide	1	4 (4.6)
Tolterodine	3	3 (3.4)
Fentanyl	1	3 (3.4)
Trazodone	1	3 (3.4)
Triamterene	1	2 (2.3)
Hydroxyzine	3	2 (2.3)
Diphenhydramine	3	2 (2.3)
Trospium	2	1 (1.1)
Dipyridamole	1	1 (1.1)
Alprazolam	1	1 (1.1)
Colchicine	1	1 (1.1)
Dicyclomine	3	1 (1.1)
Haloperidol	1	1 (1.1)
Nifedipine	1	1 (1.1)
Imipramine	3	1 (1.1)

ACB 1, mild; ACB 2, moderate; ACB 3, severe.

DISCUSSION

Engagement in activities is an important indicator of quality of life in persons with dementia. Across 775 observations, taken between 9 AM and 5 PM, residents in this sample were "asleep" or "doing nothing" more than 45% of the time. Low engagement could be affected by staffing ratios, the quality of the activity program, and resident characteristics such as untreated depression, which were not measured in this study. But the finding is typical of what others have reported in prior studies of nursing home residents' time use.[24,25] It is not unusual to find residents who are capable of independent activity to be inactive for long periods of time in the nursing home[26]; 1 year after admission to the nursing home, half of all residents were not engaged in any type of activity.[27]

Low activity engagement in nursing home residents has been associated with the presence of cognitive and physical impairments.[28] In turn, deficits in cognitive and physical performance have been associated with use of drugs with anticholinergic properties.[1,14,29,30] In this sample, residents received drugs that are not usually identified as anticholinergic, but do in fact, have central anticholinergic properties. Prescription of these drugs was extremely common in the nursing home residents who already suffer from a depleted cholinergic system: 71 (81.6%) subjects were prescribed at least 1 drug with anticholinergic properties and 32 (36.7%) were prescribed at least 1 drug with severe anticholinergic properties (ACB 3). These ACB 3 drugs have central effects equivalent to that of diphenhydramine. On average, subjects had 1.74 anticholinergic drugs prescribed and a Total ACB score of 2.55 (± 1.99).

The ACB reported here is higher than what others have reported in less vulnerable, cognitively intact community-dwelling elders. In those populations, reported rates of prescription for drugs with anticholinergic properties varied between 25% and 60% of the sample.[3,31] The magnitude of burden was also higher in this sample compared with studies of community-dwelling elders. In a report of 3013 older adults attending urban primary care clinics, the mean Total ACB score was 1.9 (± 2.4).[17] In a second sample of 249 older adults attending geriatric or primary care clinics, who were assessed using the Anticholinergic Rating Scale, a tool similar to the ACB and one that uses the same 3-point metric,[16] total burden ranged from 0.7 to 1.4 and was associated with increased risk of peripheral and central anticholinergic effects.

The presence of dementia in the subjects who comprised this sample makes the high prevalence of anticholinergic drug use troubling, as some data indicate that anticholinergic drugs may be counteractive to the drugs used to treat dementia,[4] and are known to be associated with delirium, falls, and other geriatric syndromes.[32] Although subjects were screened for acute medical conditions, some of the daytime sleep and inactivity observed may have been a result of sedation, confusion, or a hypoactive form of delirium, all of which have been associated with use of anticholinergic drugs. Larger prospective studies are needed to further assess the long-term

effects of these drugs using meaningful patient outcomes such as engagement, functional status, and cognitive decline.

Despite the high prevalence of anticholinergic drug prescription and burden observed, there was no association between ACB scores and engagement. There are a number of reasons that may explain this counterintuitive finding. First, our engagement observation period spanned only 40 minutes per day (8% of daytime) and there is a possibility that given a longer observation period we may have been able to detect differences between subjects who carried high and low anticholinergic burdens. Our observation periods were, however, individually selected to help ensure standard measurement times across subjects. The use of more intense measurement designs in future studies would capture subjects' pattern of variability in engagement over a range of time periods and may be a more informative outcome variable than a selected point in time, a limitation of the study.

Second, ability to engage in activities may not be affected by ACB if there is sufficient stimulation in the environment to overcome the central effects of these drugs. Neither environmental stimulation nor staffing ratio was measured in this study. Some drugs that carry an ACB may in fact facilitate engagement by managing symptoms that interfere with physical and social function. There is a need for research that demonstrates how nonpharmacological and pharmacological interventions can be used as complementary treatments for common symptoms in dementia.

Third, there is obviously limited precision in the categorization of anticholinergic activity using a 3-point scale. However, a dose-weighting scheme for classifying anticholinergic activity, using a tool similar to the ACB, did not lead to a significant increase in the amount of variance explained in SAA.[15] There are large individual differences in absorption, distribution, metabolism, and excretion of drug metabolites. Assessment of burden based on prescription does not take into consideration this individual variability. A lack of ability to measure this variability may account for the nonsignificant findings in this study.

Finally, while mental status and physical function were controlled in the analysis, the subjects in the sample had moderate to severe cognitive and physical impairments, so the potential exists for the disease itself to exert a more potent influence on engagement than the drugs prescribed. The findings in this study are similar to those of Sink and colleagues,[4] who noted a lack of association between anticholinergic drug use and the MDS Cognition scale in lower-functioning patients with dementia. Given the cross-sectional nature of the data it is not possible to disentangle the effects of disease-related loss of function from that caused by anticholinergic drugs. The ACB Scale may be more sensitive to quality of life indicators in earlier stages of dementia, a time when the effects of disease on functional status are less prominent, and when the effects of anticholinergic burden may be easier to discern.

This is an initial study using the ACB Scale, and further large scale studies with more intense measurement designs are needed to validate its utility. Despite limitations, this study has several strengths including the prospective design, the direct observational method for measuring engagement, and the use of a scale for ACB that was developed by a panel of geriatric clinical experts. The findings also have important implications for the care of persons with dementia. The ACB Scale has utility as a tool to alert practitioners to high anticholinergic burden in nursing home residents, and who can then use this information when choosing between equally efficacious medications. In this way the tool will help practitioners avert potential problems stemming from ACB burden in a population that is clearly at risk for poor quality of life.

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