

Anticholinergic Exposure During Rehabilitation: Cognitive and Physical Function Outcomes in Patients with Delirium Superimposed on Dementia

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Objectives: *We examined the association between anticholinergic medication exposure and subsequent cognitive and physical function in patients with delirium superimposed on dementia during rehabilitation. We also examined length of stay and discharge disposition by anticholinergic medication exposure. Design:* *In this secondary analysis we used control group data from an ongoing randomized clinical trial. Setting/Participants:* *Participants with delirium and dementia were enrolled at admission to post-acute care. These 99 participants had a mean age of 86.11 (± 6.83) years; 67.6% were women; 98% were Caucasian; and 33% were positive for at least one APOE e4 allele. Measures:* *We obtained daily measures of cognitive and physical function using: Digit Span; memory, orientation and attention items from the Montreal Cognitive Assessment; CLOX; the Confusion Assessment Method; and the Barthel Index. Anticholinergic medication exposure was measured weekly using the Anticholinergic Cognitive Burden Scale. Results:* *Using multilevel models for time we found that greater use of clinically relevant anticholinergic medications in the previous week reduced cognitive and physical function, as measured by Digit Span Backwards and the Barthel index, in the current week. There was no effect of anticholinergic medication use on delirium severity, and APOE status did not moderate any outcomes. Greater use of clinically relevant anticholinergic medications was related to longer length of stay but not discharge disposition. Conclusions:* *For vulnerable older adults, anticholinergic exposure represents a potentially modifiable risk factor for poor attention, working memory, physical function, and greater length of stay during rehabilitation. (Am J Geriatr Psychiatry 2015; 23:1250–1258)*

Key Words: Anticholinergic exposure, cognition, physical function, post-acute care, dementia

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Medications with anticholinergic effects are prescribed for many clinical problems common to older adults. It is estimated that between 20% and 50% of older adults take at least one medication with anticholinergic effects to manage a variety of medical and psychiatric symptoms such as urine incontinence, depression, or insomnia.¹ In addition to their beneficial effects, these medications have clinically relevant adverse effects that impact the central nervous system.¹ A recent systematic review of 46 studies evaluated these effects in 60,944 participants and found strong evidence for an association between increased anticholinergic exposure and deteriorating cognition, and consistent evidence for an association with a decline in physical function.² The association with delirium and mortality was inconclusive. Despite appreciable risks, the proportion of older adults prescribed anticholinergic medications has actually increased between 1995 and 2010.³

Older adults with dementia have lower cholinergic activity than those with normal cognition making them potentially more sensitive to anticholinergic medications.⁴ They are also more likely to be carriers of the APOE e 4 allele than the general population. In some studies,⁵ but not others,⁶ APOE e 4 allele carriers were found to have a greater sensitivity to anticholinergic medications.

The adverse effects of anticholinergic medications on community-dwelling,^{7,8} hospitalized,⁹ and institutionalized^{4,10} older adults with dementia have been described. We did not find any studies that examined the effects of anticholinergic medication exposure on cognitive and physical function in older adults with dementia in post-acute care settings. This was surprising given the growing number of people with dementia who require rehabilitation following hospitalization and the strong emphasis on functional outcomes in these settings. Data indicate that patients with dementia benefit from post-acute care and can experience significant functional improvements over their admission status.¹¹

Patients with dementia who receive rehabilitation following an acute medical event have complex medical and psychiatric comorbidity that may interfere with their recovery such as urine incontinence, depression, insomnia, pain, and gastrointestinal symptoms. The management of this comorbidity may include prescribing medications with anticholinergic activities such as oxybutynin for urine incontinence, paroxetine

for major depression, or diphenhydramine for insomnia. In the case of depression, the use of antidepressants may be life-saving. In the case of delirium, however, the evidence for use of antipsychotic medications outside of intensive care settings is weak.¹²

The purpose of this study was to examine the association between anticholinergic medication exposure and subsequent cognitive (attention, memory, orientation, executive function, and delirium) and physical function in patients with delirium superimposed on dementia who receive rehabilitation in post-acute care settings. We explore the moderating effect of APOE status on the association of anticholinergic medication exposure to functional outcomes because the evidence is not consistent in the literature. Delirium superimposed on dementia is common on admission to post-acute care settings and may compromise rehabilitation goals.¹² Thus we examine length of stay and discharge disposition by anticholinergic medication exposure.

METHODS

Data from an ongoing randomized clinical trial were used to address the aim of the study ([ClinicalTrials.gov](https://clinicaltrials.gov) identifier: NCT01267682). The efficacy of cognitively stimulating activities for resolving delirium in patients with dementia during rehabilitation is being tested in that trial. The protocol received institutional review board approval and was published.¹³

Setting and Sample

Participants were recruited and enrolled at the time of admission to one of eight skilled nursing facilities located in central and northeast Pennsylvania that provide post-acute care. All admissions to each facility followed an inpatient hospitalization.

Eligible participants were those 65 years of age or older, community-dwelling prior to hospitalization, having a knowledgeable informant, and having both dementia and delirium on admission to the post-acute care facility. The diagnosis of dementia was based on a Modified Blessed Dementia Rating Scale¹⁴ score of 3 or greater and a Clinical Dementia Rating¹⁵ score ranging from 0.5 to 2.0, indicating

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