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ANTICHOLINERGIC BURDEN IN OLDER ADULTS WITH MILD COGNITIVE IMPAIRMENT

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To the Editor

Higher cumulative use of medications with anticholinergic effects is associated with increased risk of incident dementia.¹ Anticholinergic drugs are prescribed to older adults for many indications, including urinary incontinence and depression. Delaying the onset of dementia by 1 year would result in 9.2 million fewer cases by 2050.² Reducing anticholinergic burden could have enormous public health implications.

Mild cognitive impairment (MCI), objective cognitive deficits without functional deficits, is present in 22% of community-dwelling adults 71 years and older.³ Those with MCI develop dementia at a higher rate than those with normal cognition.³ However, some individuals with

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MCI may revert to normal cognition, highlighting the importance of identifying modifiable risk factors for dementia among individuals with MCI.³ Previous studies have not focused on cumulative anticholinergic burden arising from multiple medicines with anticholinergic effects in persons with MCI. We investigated the prevalence of anticholinergic medicines in community-dwelling patients with MCI and identified medicines that make the greatest contribution to anticholinergic burden.

METHODS

Data were derived from the National Alzheimer's Coordinating Center Uniform Data Set (UDS), collected from September 2005 through March 2015.⁴ The data include participants with normal cognition, MCI and dementia who are assessed longitudinally at one of 34 Alzheimer's Disease Centers.⁴ We included participants who were, at baseline, aged 65 and community-dwelling. Each participant, including those with normal cognition, has an informant, usually a relative or close friend, who serves as the study partner during assessments. Annual, in-person assessments are conducted by research-trained clinicians.

Diagnosis of MCI is adjudicated by an experienced clinician or interdisciplinary team, based on the patient's history and performance on neuropsychological testing.⁵ Research staff ask the participant and informant to name all prescription and nonprescription drugs taken by the participant within the 2 weeks prior to each assessment. Depressive symptoms are assessed with the Geriatric Depression Scale and functional status with the Functional Assessment Questionnaire.⁴ Comorbidities are self-reported.⁴

Anticholinergic burden was measured using the Anticholinergic Cognitive Burden (ACB) scale. Each medicine is rated from 1 to 3 (1 = possible anticholinergic cognitive effects; 2 and 3 = definite anticholinergic cognitive effects).⁶ The total score is the sum of ACB scores of all medications taken by a participant. Analyses were performed at the last visit for each participant. Univariate analysis was performed using ANOVA for continuous data and chi-squared analysis for categorical data.

RESULTS

A total of 24,106 participants were included. Of these, 4,381 (18%) had MCI at their last visit. Participants with MCI took an average of 6.8 (SD 4.2) medicines. High ACB scores were those 2 (the top quartile for all 24,106 participants). Among participants with MCI, 1,265 (29%) had high ACB scores. Compared with the group with ACB scores <2, participants with high scores were older, had greater depressive symptomatology, poorer functional status, more comorbidities, and a higher total number of medications (all $P < .001$).

Half (50%, $n = 638$) of participants with MCI and ACB scores 2 had high ACB scores due to the additive effect of multiple possible anticholinergics (ACB Level 1). The remaining 50% of participants with MCI and ACB scores 2 were taking at least one definite anticholinergic (ACB Level 2 or 3). Among participants with MCI and ACB scores 2, metoprolol, furosemide, and warfarin were the most frequently used medications on the ACB scale (Table 1). Several definite anticholinergics (ACB Level 3) medications were also

among the most commonly used medications on the ACB scale among participants with MCI and ACB scores ≥ 2 .

DISCUSSION

Nearly one-third of patients with MCI had high ACB scores. A substantial portion of anticholinergic burden resulted from exposure to multiple possible anticholinergics (ACB Level 1). Use of definite anticholinergics was also common among participants with MCI. This use is despite growing evidence of anticholinergic-induced adverse cognitive effects, including incident dementia.¹ Limitations include the reliance on self-reported medication use, and the use of a referral-based cohort, which may limit generalizability.

Clinicians may not realize that patients using multiple medicines with possible anticholinergic effects may be at risk of adverse cognitive outcomes due to cumulative anticholinergic burden. The recent Choosing Wisely initiative advises against prescribing medications to older adults without conducting a drug regimen review.⁷ Before prescribing a new medication, clinicians should also assess the patient's cognition. If an anticholinergic medicine must be used, patients should be monitored carefully for adverse cognitive effects.

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References

1. Gray SL, Anderson ML, Dublin S, et al. Cumulative use of strong anticholinergics and incident dementia: A prospective cohort study. *JAMA Intern Med.* 2015; 175:401–407. [PubMed: 25621434]
2. Brookmeyer R, Johnson E, Ziegler-Graham K, et al. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement.* 2007; 3:186–191. [PubMed: 19595937]
3. Campbell NL, Unverzagt F, LaMantia MA, et al. Risk factors for the progression of mild cognitive impairment to dementia. *Clin Geriatr Med.* 2013; 29:873–893. [PubMed: 24094301]
4. Morris JC, Weintraub S, Chui HC, et al. The Uniform Data Set (UDS): Clinical and cognitive variables and descriptive data from Alzheimer Disease Centers. *Alzheimer Dis Assoc Disord.* 2006; 20:210–216. [PubMed: 17132964]
5. Weintraub S, Salmon D, Mercaldo N, et al. The Alzheimer's Disease Centers' Uniform Data Set (UDS): The neuropsychologic test battery. *Alzheimer Dis Assoc Disord.* 2009; 23:91–101. [PubMed: 19474567]
6. Campbell N, Boustani M, Limbil T, et al. The cognitive impact of anticholinergics: A clinical review. *Clin Interv Aging.* 2009; 4:225–233. [PubMed: 19554093]
7. AGS Choosing Wisely Workgroup. American Geriatrics Society identifies another five things that healthcare providers and patients should question. *J Am Geriatr Soc.* 2014; 62:950–960. [PubMed: 24575770]

Table 1

Twenty Most Commonly Used Anticholinergic Medications Among 1,265 Patients with MCI and High Anticholinergic Burden (ACB 2)

Drug	ACB Level	Count	Percent ^a
Metoprolol	1	348	28
Furosemide	1	260	21
Warfarin	1	247	20
Atenolol	1	179	14
Oxybutynin	3	106	8
Trazodone	1	103	8
Digoxin	1	102	8
Bupropion	1	89	7
Ranitidine	1	77	6
Paroxetine	3	67	5
Tolterodine	3	60	5
Venlafaxine	1	53	4
Prednisone	1	52	4
Loratadine	1	52	4
Hydrochlorothiazide-triamterene	1	51	4
Nifedipine	1	48	4
Alprazolam	1	48	4
Meclizine	3	44	4
Diphenhydramine	3	41	3
Solifenacin	3	39	3

^aDenominator = 1,265 participants with MCI and ACB 2.