Published in final edited form as:

J Am Geriatr Soc. 2012 July ; 60(7): 1369–1370. doi:10.1111/j.1532-5415.2012.04012.x.

Potentially Inappropriate Medication Use in Mild Cognitive Impairment (MCI) Patients: Results from the Kerala Einstein Study

Richard Tsai, M.D.¹, Mohan Noone, D.M.², Beena Johnson, MBBS², Vayyattu G. Pradeep, D.M.², and Joe Verghese, MBBS.¹

¹Department of Neurology, Albert Einstein College of Medicine Bronx, NY, USA

²Department of Neurology, Baby Memorial Hospital, Kozhikode, Kerala India

To the Editor

Potentially inappropriate medication (PIM) usage is a major safety concern, especially in cognitively impaired elderly. Despite the availability of guidelines for identifying PIMs,¹ a high proportion of older adults (8%–21%) continue to receive PIM.^{2–4} Studies in developed countries suggest that patients with mild cognitive impairment (MCI) syndrome are at higher risk than the general population of receiving PIM.⁵ However, little is known about PIM usage among older adults, especially those with MCI, in developing countries. Elderly patients in developing countries have limited access to healthcare and PIMs may not only expend resources but the adverse side effects may not be readily recognized.

METHODS

We identified 27 patients with MCI (mean age 70.9, 40.7% women) attending neurology clinics at Baby Memorial Hospital, Kozhikode between October 2008 and October 2010 as part of the Kerala Einstein Study (KES).⁶ The goal of the KES is to identify risk factors for dementia in the southern Indian state of Kerala. We frequency matched cases by age and sex to 79 cognitively normal adults (mean age 70.4, 35.4% women) recruited from relatives of patients (70%) as well as from patients referred for non-cognitive complaints such as headaches, back pain, and peripheral neuropathies (30%). Inclusion criteria for KES were age 60 and older and willing to complete study procedures. Exclusion criteria included severe audiovisual loss or presence of active medical or psychiatric illness that in the judgment of the study clinician would interfere with completion of study procedures. Informed consent was obtained from all participants and study evaluations followed protocols approved by the local institutional review board.

Corresponding author: Joe Verghese, M.D., Division of Cognitive & Motor Aging, Saul R Korey Department of Neurology, Albert Einstein College of Medicine, 1165 Morris Park Avenue, Rousso 301, Bronx, New York 10461, USA. Tel: 718 430 3808. Fax: 718 430 3829. joe.verghese@einstein.yu.edu.

Conflict of Interest

Drs. Noone, Johnson, Pradeep, and Verghese have received research support from the NIH (grants 1 R21 AG025119 and 1R01 AG039330-01). Dr. Verghese has reviewed for NIH and also received funding from National Institute on Aging grants (PO1 AG03949 and R01AG036921-01A1).

Author Contributions:

Richard Tsai: study concept, data acquisition, data analysis, data interpretation, and drafting manuscript.

Mohan Noone: study design, data acquisition, data interpretation, drafting manuscript.

Beena Johnson: study design, data acquisition, data interpretation, drafting manuscript.

VG Pradeep: study design, data acquisition, data interpretation, drafting manuscript.

Joe Verghese: study design and concept, obtained grant support, data analysis, data interpretation, drafting manuscript

A neurologist, experienced in dementia evaluation, obtained medical history and recorded medication use. The clinician reviewed medication bottles, medical records, and verified information with informants. A battery of cognitive tests in the local language (Malayalam) and validated in the Kerala elderly population was administered by another clinician with behavioral neurology expertise. The cognitive battery assessed general cognition: Addenbrooke Cognitive Examination (ACE), Memory: Rey Auditory Verbal Learning Test, Attention/Executive function: Digit span test, and Mood: 15-item Geriatric Depression scale. The ACE incorporates the Mini-Mental State Examination (MMSE).

MCI was diagnosed in non-demented individuals with cognitive complaints and objective impairment (1.5 SD or below age and sex appropriate means) on tests of memory, attention executive function, or language at consensus diagnostic conferences attended by two or more study clinicians.

An independent clinician who did not do study evaluations or diagnosis reviewed medications blinded to cognitive status to identify PIM usage as per the updated 2003 Beer's criteria¹ with the addition of benzodiazepines.⁵

Descriptive statistics were used to test group differences by MCI status. Logistic regression analysis adjusted for cognitive status (MMSE), Charlson Comorbidity Index and depressive symptoms was used to further examine association of MCI with PIM.

RESULTS

Seven participants were prescribed PIM (5.6%). Patients on PIM had higher Charlson Comorbidity Index scores compared to those not on PIM (1.43 vs. 0.70, $p=0.034$). There were no significant group differences in age, education, depressive symptoms, cognitive scores, and prescription medication count.

Table 1 shows baseline and cognitive test characteristics by MCI status. The 27 MCI patients (20 amnesic and 7 non-amnesic) had higher PIM usage than the 79 normal controls (18.5% vs. 2.5%, $p=0.011$). Among MCI cases, PIMs included two medications with anti-cholinergic properties, two benzodiazepines and one cardiac glycoside. In the controls, PIMs consisted of one tricyclic antidepressant and one non-steroidal anti-inflammatory drug. MCI patients were at higher risk of being on a PIM (adjusted odds ratio 8.75; 95% CI 1.58 to 48.23).

DISCUSSION

Higher PIM use (18.5%) was seen in MCI patients in a clinic-based population from Kerala, India. Patients with MCI had an eight-fold increased risk of being on PIM compared to normal adults. A US based study of 689 MCI patients reported PIM usage in 20.8%, with anticholinergics and benzodiazepines being the most common.⁵ U.S. based studies have reported that higher prescription medication count increases risk of PIM usage,^{2,4,5} but this was not the case in our study. The lower PIM usage (5.6%) in our overall sample may be a result of cultural differences in medical or social practices as well as resource availability but is still of concern in MCI patients. The high prevalence of medications with anti-cholinergic effects is concerning as they may negatively affect cognition.⁷ Furthermore, concomitant use of cholinesterase inhibitors and anticholinergics diminishes effectiveness of dementia medications.⁸ Although limited by sample size, the results serve as a reminder that extra care be taken when managing medications for MCI patients in developing countries.

Acknowledgments

Funding: Research grant from the National Institute of Health (1 R21 AG025119 and 1R01 AG039330-01)

Sponsor's Role: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

References

1. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts. *Arch Intern Med.* 2003; 163:2716–2724. [PubMed: 14662625]
2. Zhan C, Sangl J, Bierman A, et al. Potentially Inappropriate medication use in the community-dwelling elderly: Findings from the 1996 medical expenditure panel Survey. *JAMA.* 2001; 286:2823–2829. [PubMed: 11735757]
3. Lai HY, Hwang SJ, Chen YC, et al. Prevalence of the prescribing of PIM at ambulatory care visits by elderly patients covered by the Taiwanese National Health Insurance Program. *Clin Ther.* 2009; 31:1859–1870. [PubMed: 19808145]
4. Goulding MR. Inappropriate medication prescribing for ambulatory care patients. *Arch Intern Med.* 2004; 164:305–312. [PubMed: 14769626]
5. Weston AL, Weinstein AM, Barton C, et al. Potentially inappropriate medication use in older adults with MCI. *J Gerontol A Biol Sci Med Sci.* 2010; 65:318–321. [PubMed: 19843646]
6. Ambrose AF, Noone ML, Pradeep VG, et al. Gait and cognition in older adults: Insights from the Bronx and Kerala. *Ann Indian Acad Neurol.* 2010; 13:S99–S103. [PubMed: 21369426]
7. 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]
8. Boudreau DM, Yu O, Gray SL, et al. Concomitant use of cholinesterase inhibitors and anticholinergics: Prevalence and outcomes. *J Am Geriatr Soc.* 2011; 59:2069–2076.

Table 1
Baseline Characteristics and Cognitive Test Performance by MCI Status

Values expressed as mean $\pm$ SD unless otherwise specified.

Variables	MCI (n = 27)	Normal elderly (n = 79)	P-value
Age	70.9 $\pm$ 5.9	70.4 $\pm$ 5.7	0.686
Sex, female %	40.7	35.4	0.649
Education, years	5.7 $\pm$ 3.8	8.7 $\pm$ 3.4	<0.001
Total prescription medication count	2.0 $\pm$ 0.8	1.9 $\pm$ 0.4	0.765
ACE	61.5 $\pm$ 12.0	80.7 $\pm$ 10.7	<0.001
Mini Mental Status Exam	22.9 $\pm$ 3.7	28.2 $\pm$ 2.3	<0.001
RAVLT 20 minute recall	1.5 $\pm$ 1.7	4.5 $\pm$ 2.9	<0.001
Digit span forward	5.1 $\pm$ 1.1	6.1 $\pm$ 1.1	<0.001
Digit span backward	2.6 $\pm$ 1.5	4.5 $\pm$ 4.5	0.037
Geriatric Depression Scale	6.6 $\pm$ 3.4	4.0 $\pm$ 2.9	<0.001

ACE: Addenbrooke Cognitive Examination

RAVLT: Rey Auditory Verbal Learning Test