Drug Prescribing in the Elderly Receiving Home Care

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ABSTRACT

Background: To compare the prevalence of potentially inappropriate medications (PIMs) using the 2012 and 2003 Beers Criteria in frail older patients receiving home health care services (HHS), and to explore the correlates of PIMs based on the 2012 Beers criteria.

Materials and Methods: A total of 145 older patients (mean age, 80.9 ± 7.6 years) with Barthel scale ≤ 60 receiving regular HHS from a university hospital between January 2013 and June 2013 were retrospectively enrolled. The 2003 and 2012 Beers criteria were used separately to detect PIMs. Logistic regressions, receiver-operating-characteristic curve analyses and number needed to harm were used, where appropriate.

Results: The 2012 Beers Criteria identified more PIM cases than did the 2003 Beers Criteria (66.9% versus 55.9%, P < 0.05). Multivariate analysis revealed that PIM identified by the 2012 Beers Criteria was associated with an increased number of medications prescribed (P = 0.019) and the presence of psychiatric diseases (P = 0.001). Moreover, the area under the receiver-operating-characteristic curve for the number of drugs to predict the risk of PIM was 0.674 (P < 0.001) with the optimal cutoff value of 6 medications. After adjusting for age, sex, Charlson comorbidity index and psychiatric disorders, patients taking ≥ 6 drugs (adjusted odds ratio, 2.33; adjusted number needed to harm, 3.93; P < 0.05) had a significantly higher risk for PIM than those taking < 6 drugs.

Conclusions: Our data showed that the 2012 Beers Criteria was more sensitive in detecting PIMs than the 2003 Beers Criteria. Furthermore, frail older patients receiving HHS with polymedication and with psychiatric illnesses had higher risk of PIM when using the 2012 criteria. The number of medications prescribed could be a useful index for risk stratification, and at the same time help physicians to be aware of the high risk for PIM when prescribing 6 or more drugs to frail older adults during in-home visits.

Key Indexing Terms: Inappropriate prescribing; Risk factor; Home care services; Frail elderly; Drug prescriptions.
16.9-38.0% of older patients receiving HHS; however, the criteria were criticized by some investigators who believed that this tool underestimated the use of PIMs because of the lack of drug-disease or some drug-drug interactions from the criteria and because some agents had been withdrawn from the market. The Beers Criteria were updated in 2012 to consider newly attained evidence about the efficacy and safety of various medications as well as the removal of drugs that were no longer in use. The noted differences in this updated criteria compared to the 2003 version included (1) 20 therapeutic class or medication additions or modifications (e.g., all short-acting benzodiazepines regardless of dose, glyburide, megesterol, metoclopramide and sliding scale insulin) and 7 deletions (e.g., propoxyphene, ethacrynic acid and ferrous sulfate >325 mg/day) in the updated “drugs-to-avoid” list; (2) 47 additions or modifications (e.g., acetylcholinesterase inhibitors or syncope, selective serotonin-reuptake inhibitors or falls or fractures and pioglitazone or rosiglitazone or heart failure) and 21 deletions (e.g., phenylpropanolamine or hypertension and pseudoephedrine or hypertension) in the updated “drug-disease interactions” list and (3) a new category of PIMs to be used with caution in older adults (i.e., aspirin for primary prevention of cardiac events, dabigatran and prasugrel). Additionally, the Beers Criteria would be updated regularly via the means of an evidence-based approach using the Institute of Medicine standards and the development of the multidisciplinary partnerships in geriatric medicine.

The objectives of this study, therefore, were to compare the prevalence of PIM using both the 2003 and 2012 Beers Criteria, and to identify independent correlates of the risk of PIM based on the 2012 Beers Criteria in frail older patients receiving HHS.

MATERIALS AND METHODS

Study Sample and Measures

This retrospective study was carried out at the Chung Shan Medical University Hospital, an over 1300-bed medical center, after approval was obtained from the Institutional Review Board and the requirement for informed consent was waived. In this hospital, only persons who met the qualifications for HHS according to the NHFI program by having marked dependence to accomplish activities of daily living (ADL) could apply for the services. ADL disability was based on the Barthel index (score: 0-100), and a score ≤ 60 was defined as marked dependence for ADL. Chronic diseases were defined as medical conditions that cannot spontaneously remit more than 3 months according to the NHFI program in Taiwan. If a patient's conditions were stable according to the home care physician's assessment, then a long-term prescription could be given, based on the policy of the Taiwanese NHFI Administration. We selected HHS recipients aged 60 years or older following this generally used definition of an older person by the World Health Organization. Consecutive older HHS recipients who received long-term (≥ 4 weeks) prescriptions for their chronic diseases from January 2013 to June 2013 were included in the study. For those HHS recipients who had more than 1 visit to obtain a prescription refill during the study period, only the first occasion was used in the analysis. In all, 191 persons received HHS during the study period, and 145 recipients met the criteria and were included in our study. Data from the medical record of every patient included demographic information, history details, clinical data and the drugs prescribed. These data were extracted from the medical records by a well-trained physician through an electronic medical record system of this hospital. This data abstractor was blinded to the study hypothesis, and used a standard data abstraction form to review medical records. The abstractor's performance was thoroughly monitored by a senior physician. The 2003 and 2012 Beers Criteria were applied to identify PIMs in study patients. The 2012 Beers Criteria in our study did not include the medications that should be used with caution. A total of 2 different geriatricians ascertained the PIM cases based on the 2 criteria by reviewing the computerized database of these patients. We also sampled randomly 20% of our study subjects for the interrater reliability assessment between both geriatricians by using the Kappa (κ) statistics and the interrater agreement was 100% (κ = 1.0). The Charlson comorbidity index (CCI) was used to estimate the disease severity of each patient. Categories of comorbid conditions and their corresponding International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes are summarized in Appendix A(1).

Analytical Approach and Statistical Methods

Descriptive statistics were expressed as means ± standard deviations or numbers with percentages. Student's t test or the Mann-Whitney U test was applied to compare continuous data between groups and the χ² test, McNemer test or Fisher exact test was employed to compare categorical variables between groups, where appropriate. These patients receiving HHS were separated into 2 groups—the PIM group (patients having at least 1 PIM) and the non-PIM group (those without any PIM). Logistic regression with purposeful selection of covariates was used to assess the risk factors for PIM using the 2012 Beers Criteria among the older patients receiving HHS, a method addressed by Hosmer et al. The area under the curve of the receiver-operating-characteristic curve analysis was also measured using MedCalc Statistical Software 9.5 (Broekstraat, Mariakerke, Belgium). A post hoc power based on the method of Hanley and McNeil was used to estimate for the receiver-operating-characteristic curve analysis. The optimal cutoff point was based on the Youden index (the maximum value of sensitivity + specificity = 1). Sensitivity,
specificity, positive predictive values (PPV) and negative predictive values were computed according to the optimal cutoff value for the number of medications prescribed in predicting PIM using the 2012 Beers Criteria. Because the baseline variables, including age, sex and severity of illness, could be associated with PIM in the literature, the significant factor(s) identified by the aforementioned logistic regression as well as the baseline variables were regarded as covariates for assessing the effect of number of medications prescribed on the risk of PIM. The number needed to harm (NNH) was calculated to estimate the effect of the number of medications prescribed on the risk of PIM using the adjusted odds ratio (OR) through a logistic regression model; the equation was as follows: adjusted NNH = 1/[(adjusted OR - 1) × [event rate in the reference group]] + adjusted OR/[adjusted OR - 1] × [event rate in the nonreference group].

RESULTS

For the 145 older HHS recipients recruited, their mean age was 80.9 ± 7.6 years (range: 60-96 years), 47.6% were men and 95.2% were totally dependent for ADL (Barthel score ≤ 20). The mean CCI score was 4.2 ± 2.2 (range: 0-13). The mean numbers of medicines prescribed and coexisting disorders were 7.7 ± 3.4 and 7.6 ± 3.6, respectively. Among these systemic disorders, the most common coexisting specific disease was hypertension (n = 104), followed by strokes (n = 81), chronic kidney injury (n = 76) and type 2 diabetes mellitus (n = 62). Among the 145 older HHS recipients, the 2012 Beers Criteria identified more PIM cases than did the 2003 Beers Criteria (97 patients [66.9%] versus 81 patients [55.9%], P < 0.05). Among the patients taking PIM identified by either the 2003 or 2012 Beers Criteria, 15 were identified only by the 2003 Beers Criteria, 31 were identified only by the 2012 Beers Criteria and 66 were identified by both the criteria. The patients taking PIM identified by the 2012 Beers Criteria had more instances of PIM than those identified by the 2003 Beers Criteria (2.5 ± 1.8 versus 2.0 ± 1.3, P < 0.05). According to both the 2003 and 2012 Beers Criteria, PIM groups had more medicines prescribed and more coexisting disorders than non-PIM groups (all P < 0.01). Based on the 2012 Beers Criteria, the PIM group had a higher frequency of neurologic or psychiatric disorders compared with the non-PIM group (both P < 0.05), whereas no difference in comorbid conditions was seen on the basis of the 2003 Beers Criteria (Table 1). According to the 2003 Beers Criteria, calcium channel blockers (CCBs) were the most frequently prescribed PIMs (25 instances in 22 patients), whereas based on the 2012 Beers Criteria, benzodiazepines and nonbenzodiazepine hypnotics were the most commonly prescribed PIMs (43 instances in 28 patients); Ergot mesylates and dipyridamole were the next most common based on both the 2003 and 2012 Beers Criteria (Table 2; details in Appendix A2 and 3).

On multivariate analysis, an increased number of medicines prescribed (P = 0.019) and the presence of psychiatric disorders (P = 0.001) were associated with the use of PIMs based on the 2012 Beers Criteria (Table 3). The area under the curve for the number of medicines prescribed was 0.674 (95% CI: 0.591-0.750; P < 0.001; post hoc power = 0.948) in predicting the PIM risk. At the cutoff value of ≥6 medications prescribed (the optimal cutoff value being determined by Youden’s index), the model had a sensitivity of 81%, a specificity of 42%, PPV of 74% and negative predictive value of 53%. A multivariate logistic regression analysis was then performed to assess the effect of drug numbers relative to PIM risk, based on the 2012 Beers Criteria, between the 2 patient groups (patients having <6 drugs prescribed and those taking ≥6 drugs) by adjusting for baseline variables (age, sex and CCI) and the other risk factor (the presence of psychiatric disorders) identified from the multivariate analysis. After adjustment for covariates, older patients receiving HHS having ≥6 drugs prescribed had significantly higher risks for PIM when compared with those taking <6 drugs (adjusted OR, 2.33; 95% CI: 1.04-5.21; P < 0.05). The estimated NNH was 3.93 for the group having ≥6 drugs prescribed when the harmful effect of those taking <6 drugs prescribed was assumed to be zero (Table 4).

DISCUSSION

There were 2 key findings in our study. First, the 2012 Beers Criteria identified significantly more instances of PIM and a higher prevalence of PIM in frail older adults receiving HHS than the 2003 Beers Criteria did. This finding supported several authors’ appraisals of the 2003 Beers Criteria that the estimate of prevalence of PIM use in older people would be conservative and even underrated when using these criteria. Second, the risk of PIM use, based on the 2012 Beers Criteria, increased when additional drugs were prescribed and in the presence of psychiatric diseases in frail older patients receiving HHS. Our results confirmed earlier reports using the older Beers criteria that multiple drug prescriptions were an important predictor of the use of PIMs for older people; however, the smallest number of medications needed to be treated as polymedication among older patients receiving HHS remains debatable in the literature, and it ranges from 4-20 different drugs. The number of prescribed
medications in the present study displayed a significantly discriminatory ability to predict the risk of PIM among older patients receiving HHS and also determined a cutoff number of ≥6 prescription drugs with a modest sensitivity and PPV in the prediction model. We further estimated that under the updated Beers criteria, for a suppositional group of 1000 older patients receiving HHS, 6 or more prescription medications would be expected to cause approximately 254 persons to have harmful effects from PIMs (estimated NNH = 3.93) when <6 drugs were assumed to be harmless. This finding provides meaningful clinical-based data regarding the effect of the number of drugs prescribed on the risk of PIM among frail older adults receiving HHS.

There were potential limitations in this study. The inferences from our results may be limited by the cross-sectional nature of the study and a single medical institution. Owing to the lack of each patient’s data regarding subsequent health event(s), the effect of PIM on adverse outcomes caused by adverse drug events cannot be assessed in the present study; a further follow-up study should be conducted. The information regarding over-the-counter drugs, dietary supplements and traditional Chinese herbs used by our patients receiving HHS was not available, and this might have led to an underestimation of the risk of PIMs. As the NHI program is obligatory for people in Taiwan, all study patients’ prescriptions were covered by this program, thereby minimizing the likelihood of over-the-counter

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n = 145)</th>
<th>Beers Criteria 2003</th>
<th>Beers Criteria 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PIM (n = 81)</td>
<td>Non-PIM (n = 64)</td>
<td>PIM (n = 97)</td>
</tr>
<tr>
<td>Instance of PIM/person</td>
<td>2.0 ± 1.3</td>
<td>2.5 ± 1.8</td>
<td>2.5 ± 1.8</td>
</tr>
<tr>
<td>Age (years)</td>
<td>80.9 ± 7.6</td>
<td>81.3 ± 8.0</td>
<td>80.4 ± 7.1</td>
</tr>
<tr>
<td>Sex, male</td>
<td>69 (47.6)</td>
<td>37 (54.5)</td>
<td>32 (50.0)</td>
</tr>
<tr>
<td>CCI (points)</td>
<td>4.2 ± 2.2</td>
<td>4.5 ± 2.3</td>
<td>3.8 ± 1.9</td>
</tr>
<tr>
<td>Barthel index ≤20 points</td>
<td>138 (95.2)</td>
<td>75 (92.6)</td>
<td>63 (98.4)</td>
</tr>
<tr>
<td>Number of prescribed medications</td>
<td>7.7 ± 3.4</td>
<td>8.3 ± 3.6</td>
<td>6.8 ± 3.0</td>
</tr>
<tr>
<td>Number of coexisting disorders</td>
<td>7.6 ± 3.6</td>
<td>8.4 ± 3.8</td>
<td>6.6 ± 3.1</td>
</tr>
</tbody>
</table>

CCI, Charlson comorbidity index; HHS, home health care services; PIM, potentially inappropriate medication.

All data are expressed as number (%) or mean ± standard deviation.

* Patients who fit into more than 1 category were counted in each.

** P < 0.05, comparing the instances of PIM/person between the 2 criteria.

*** P < 0.05, a comparison of the PIM and non-PIM groups based on the 2003 Beers Criteria.

**** P < 0.05, a comparison of the PIM and non-PIM groups based on the 2012 Beers Criteria.

### TABLE 2. The 5 most frequent PIMs based on the 2003 and 2012 Beers Criteria.

<table>
<thead>
<tr>
<th>(A) Therapeutic category or drug based on the 2003 Beers Criteria</th>
<th>PIM patients (n = 81) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium channel blockers</td>
<td>22 (25.9)</td>
</tr>
<tr>
<td>Ergot mesylates</td>
<td>17 (21.0)</td>
</tr>
<tr>
<td>Dipyridamole, oral short acting</td>
<td>14 (17.3)</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>12 (14.8)</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>10 (12.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(B) Therapeutic category or drug based on the 2012 Beers Criteria</th>
<th>PIM patients (n = 97) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting, intermediate-acting and long-acting benzodiazepines and nonbenzodiazepine hypnotics</td>
<td>28 (28.9)</td>
</tr>
<tr>
<td>Ergot mesylates</td>
<td>17 (17.5)</td>
</tr>
<tr>
<td>Dipyridamole, oral short acting</td>
<td>14 (14.4)</td>
</tr>
<tr>
<td>Antipsychotics (first-generation and second-generation)</td>
<td>14 (14.4)</td>
</tr>
<tr>
<td>First-generation antihistamines</td>
<td>11 (11.3)</td>
</tr>
</tbody>
</table>

PIM, potentially inappropriate medication.

a Patients who fit into more than 1 category were counted in each.

b Including only chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine, triprolamine and dextromethorphan.
medication use. Moreover, the information involving comorbid conditions for every case was extracted from the patients’ medical records and was unlike the fashion of several previous reports only based on the disease codes of the patients’ electronic record, making our findings more dependable.

In the present study, the prevalence of PIM based on the 2003 Beers Criteria was 55.9%, a finding higher than that in previous reports involving older patients receiving HHS and using the same criteria. This may have resulted from the fact that our HHS recipients had complex chronic illnesses with almost total dependence for ADL and were more frail than those in previous reports. The 2012 Beers Criteria identified PIM in a higher proportion of participants (66.9%) than the 2003 criteria. The differences in the medication lists, particularly 65 additions or modifications and only 28 deletions among drug classes or condition categories in the 2012 criteria and prescription preferences in some medical conditions in the patients receiving HHS may account for the variation in the prevalence of PIMs between the 2 sets of criteria. In the 2012 criteria, all benzodiazepines and first-generation and second-generation antipsychotic agents and all types of benzodiazepines, which were the most frequently prescribed PIMs detected by the updated criteria in our patients, are explicitly listed; however, in the 2003 criteria this information is absent and there is no report on dose limits of short-acting and intermediate-acting benzodiazepines. Additionally, non-benzodiazepines (Z-hypnotics), which were not part of the 2003 criteria, are increasingly used in the treatment of insomnia, and have been reported to cause adverse events similar to those of benzodiazepines in the elderly. These PIM-related psychotropic agents identified by the 2012 Beers Criteria were commonly seen among our older patients receiving HHS; this may explain why psychiatric illness had an independent effect on the risks of PIM, a result concordant with previous PIM-related studies. Chronic constipation as a result of the use of dihydropyridine CCBs is no longer regarded as a PIM in the updated Beers Criteria because the benefits of their use outweigh their disadvantages in older adults with heart disease, and the incidence of constipation among older people using dihydropyridine CCBs is rare when compared to that in those taking nondihydropyridine CCBs. However, all CCBs may trigger constipation, and clinicians should consider an alternative agent if constipation develops or chronic constipation becomes worse. Ergot (Ergoloid) mesylates and dipyridamol were 2 of the 3 most frequent PIMs, based on both the 2003 and 2012 Beers Criteria, a finding similar to those in previously published studies involving PIM. This suggests that it cannot be overemphasized that continuing education for physicians should include appropriate prescribing practices.

In the present study, older patients receiving HHS with a cutoff drug number of ≥6 bore a higher risk of PIM compared with those using <6 drugs, indicating that reduction of the PIM prescribed is of great concern to clinical practitioners. The HHS in Taiwan is usually provided by family or internal physicians and home care nurses. Educational programs for these health care providers as well as the related administrative regulations in the NHI program seem to be a reasonable option to improve the selection of prescription drugs, to diminish the PIM use and to save the expenditure of medications. Although the Beers Criteria and other PIM-related explicit lists can be used as a tool to assess medication appropriateness, these criteria are complex and not easy to use; in addition, these criteria are regularly updated based on the new evidence for PIMs lists to be assessed routinely, thereby hindering physicians from applying these criteria in their busy practices. Less expenditure of time and effort is crucial when a PIM-related list is considered for use in routine practice. The use of e-prescribing systems and other forms of technology, such as electronic prescribing

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**TABLE 3.** Factors relevant to the risk of PIM according to the 2012 Beers Criteria.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Multivariate analysis</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Number of prescribed medications</td>
<td>1.15 (1.01-1.32)</td>
<td>0.019</td>
</tr>
<tr>
<td>Psychiatric disorder</td>
<td>5.43 (1.94-15.19)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

OR, odds ratio; PIM, potentially inappropriate medication.

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**TABLE 4.** Sensitivity, specificity, predictive values, odds ratio and estimated number needed to harm for the optimal cutoff value of the number of prescribed medications in predicting the risk of PIM according to the 2012 Beers Criteria in 145 older adults receiving HHS.

<table>
<thead>
<tr>
<th>Number of drugs</th>
<th>PIM (n = 97) (%)</th>
<th>Non-PIM (n = 48) (%)</th>
<th>Sens (%) (95% CI)</th>
<th>Spec (%) (95% CI)</th>
<th>PPV (%) (95% CI)</th>
<th>NPV (%) (95% CI)</th>
<th>Adjusted OR* (95% CI)</th>
<th>eNNH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥6</td>
<td>79 (81.4)</td>
<td>28 (58.3)</td>
<td>81 (72-89)</td>
<td>42 (28-57)</td>
<td>74 (64-82)</td>
<td>53 (36-69)</td>
<td>2.33 (1.04-5.21)</td>
<td>3.93 (2.18-7.99)</td>
</tr>
</tbody>
</table>

HHS, home health care services; eNNH, estimated number needed to harm; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value; Sen, sensitivity; Spe, specificity.

* Adjusted for age, sex, severity of comorbid conditions and history of psychiatric disorders.

** The optimal cutoff value was estimated according to Youden’s index.
alerts and computer-generated reminders, to reduce inappropriate prescribing in older patients, is more accepted as a tool for health care professionals and has been reported to diminish the risk of PIM in older people.34,35 However, these e-prescribing modules may be expensive or not accessible to medical facilities with inadequate resources, particularly in undeveloped and less-developed countries. Our findings would suggest a prompt stratification of the risk of PIM in older HHS recipients at the time of a home visit, as it makes clinicians aware of the high likelihood of PIM when the old person is taking 6 or more drugs.

CONCLUSIONS

Our study revealed that the 2012 Beers Criteria was more sensitive in detecting PIMs than the 2003 Beers Criteria. Furthermore, frail older patients receiving HHS with polymedication and with psychiatric illnesses were found to have higher risk of PIM when using the 2012 criteria. The number of medications prescribed could be a useful index for risk stratification, and remind physicians of the high risk for PIM use when prescribing 6 or more drugs to frail older adults during in-home visits.

Appendix A. Supplementary Information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.amjms.2016.04.015.

REFERENCES


From the Institute of Medicine (CHT, MCW, HCL, DBL, MCL, SCC) and School of Medicine (CHT, CFT, YTL, CCC, MCL, SCC) and School of Medical Laboratory and Biotechnology (DBL) and Center for Education and Research on Geriatrics and Gerontology (CCC, MCL, SCC), Chung Shan Medical University, Taichung, Taiwan; Department of Otolaryngology (CHT) and Department of Family and Community Medicine (MCW, CCC, SCC) and Department of Internal Medicine (CFT, YTL) and Department of Pharmacy (HCL), Chung Shan Medical University Hospital, Taichung, Taiwan; Department of Family Medicine (MCW, MCL), Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan.

The authors have no financial or other conflicts of interest to disclose.

Submitted November 5, 2015; accepted April 8, 2016.

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