

Polypharmacy leads to increased prevalence of potentially inappropriate medication in the Indonesian geriatric population visiting primary care facilities

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Background: The geriatric population is particularly vulnerable to being prescribed potentially inappropriate medication (PIM); however, the prevalence of this occurrence remains poorly investigated in Indonesia. Thus in this research, we focused on investigating the prevalence and predictors of PIM among the Indonesian geriatric population in a primary health care setting.

Methods: A retrospective observational study was conducted in 25 primary health care facilities in Karawang District, Indonesia. The medical prescriptions of patients aged ≥ 60 years during January–December 2014 were documented, and the PIM was assessed based on Beers and McLeod criteria. The influence of age, sex, number of diseases, and polypharmacy toward PIM was assessed using a logistic regression model. A P -value of <0.05 defined statistical significance.

Results: A total of 3,819 subjects were included in the study. PIM was highly prevalent (52.2%) among the Indonesian elderly. Chlorpheniramine, mefenamic acid, ibuprofen, and nifedipine were the most commonly prescribed PIM. Polypharmacy (odds ratio: 1.2 [0.6, 2.1]) was the only factor associated with the use of PIM, while sex, age, and multiple diseases did not show significant association.

Conclusion: PIM is a concern in the Indonesian geriatric population. Health care professionals are encouraged to review the medications of their geriatric patients using updated safety guidelines to prevent risks associated with PIM.

Keywords: potentially inappropriate medication, polypharmacy, geriatrics, adverse drug reactions, hospitalization

Introduction

The use of potentially inappropriate medication (PIM) is a major safety concern with serious health consequences.^{1,2} PIM encompasses the use of medication for which the risks outweigh the benefits, particularly when there is evidence of available alternative therapies that are safer and equally or more effective.³ It also includes the misuse of medicines, including inappropriate dose and duration.⁴

The geriatric population is at risk for PIM prescription. The existence of multiple comorbid conditions and altered pharmacokinetics and pharmacodynamics render this age group particularly vulnerable to inappropriate prescribing.^{5,6} Previous studies showed that the use of PIM in a geriatric population was associated with adverse drug reactions (ADRs), hospital admission, and mortality.^{7–10}

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Several assessment tools have been developed to detect inappropriate prescribing for the geriatric population, either based on implicit or explicit judgments.^{11–15} Unlike the implicit tools (eg, physicians assessment), the latter is more reproducible and is easier to apply in large-scale studies with minimal financial burden.¹⁶ One of the most widely used explicit tools with international acceptance is Beers criteria. It consists of a list of 53 inappropriate drugs that should be avoided by geriatric patients.¹⁷ Another criteria developed by Canadian consensus, the McLeod et al¹⁸ criteria, describes prescribing guidelines with clinical relevance for medications in the geriatric population.

There are numerous reports on the evaluation of PIM prescription and its predictors among the geriatric population in various regions. A review of studies conducted in Europe and the United States revealed that the prevalence of PIM reached 40%.¹⁹ In Brazil, 46.2% of total patients encounters used PIM.²⁰ Within Asian countries, the prevalence of PIM was 21.1% and 32.7%, in Japan and Malaysia, respectively.^{21,22}

Indonesia is a country with a geriatric population that is growing at a rapid rate.²³ However, there is very limited information regarding PIM use among the Indonesian geriatric population, particularly in primary health care facilities. Primary health care is the setting in which most Indonesian geriatric patients receive their medical care, particularly medication for chronic illnesses. Improving the quality of prescribing in primary health care is important to reduce preventable harm and unnecessary hospitalizations.²⁴ Therefore, this study aimed to assess the prevalence and the predictors of PIM prescription among the Indonesian geriatric population visiting primary health care facilities in Karawang District, using Beers and McLeod criteria.

Methods

Study design

This was a retrospective observational study conducted at 25 primary health care facilities in Karawang District, Indonesia. The data source included both acute and chronic medical prescription records of the patients aged ≥ 60 years during January–December 2014. There are varying definitions of the elderly, which may be due to differences of life expectancy in different geographic regions. We used the cut-off 60 years based on the recommendation of World Health Organization regional office for South-East Asia.²⁵

Assuming a prevalence rate of 20.4%,²⁶ a minimum sample size of 662 was required (95% confidence level). The simple random sampling method was employed to select the

study subjects. For each, the following data were obtained and documented: demographic characteristics, all prescribed medications with doses, and diagnoses.

The data accessed in this study were deidentified to protect the patients identity. This study was approved by the Health Research Ethics Committee of Universitas Padjadjaran, Indonesia, No 777/UN6.C1.3.2/KEPK/PN/2015. Informed consent of participants was not required as the retrospective study design did not affect the health care of included patients.

PIM criteria

Prescribing of PIM was evaluated using the updated Beers and McLeod criteria.^{17,18} The 2012 updated Beers criteria identified categories of drugs that should be avoided by geriatric populations, drugs that should be avoided in certain medical conditions, and drugs that should be used with caution. In this study, the assessment was based on the first set of criteria, as it has broad and straightforward application, which consists of 38 medications.¹⁷ In the McLeod guideline, we adopted the criteria related to drugs and doses that should be avoided by the geriatric population.¹⁸ Prevalence of PIM was calculated based on the number of patients with at least one PIM criteria in their medical prescription. The complete list of Beers and McLeod drugs criteria that used in this study can be seen in Table 1.

Data analysis

The percentage of prescriptions consisting of at least one PIM, either from Beers or McLeod criteria, was calculated. The pattern of the PIM was also recorded. We examined the association between age, sex, number of diseases, and number of medications toward PIM using a logistic regression model. Polypharmacy was defined by the use of ≥ 5 medications.^{27,28} The results are expressed as odds ratios (ORs) with 95% CI. Statistical significance was set at <0.05 . Analysis was performed using Stata 11.2 (Stata Corp, College Station, TX, USA).

Results

During the study period, 6,519 records were selected. We excluded 2,700 records due to incomplete data for analysis. As presented in Table 2, a total of 3,819 subjects was included in this study. The mean age was 65.8 years old (SD 6.2), and the dominant group was female. The average number of diseases was 1.2 (SD 0.4). The number of drugs per record was in the range of 1–6, with an average of 3.3 (SD 0.8).

Table 1 Criteria used to identify PIM based on Beers and McLeod et al criteria

| Drugs | Beers | McLeod | Beers and McLeod |
|---------------------------------|-------|--------|------------------|
| Anticholinergics | | | |
| Brompheniramine | ✓ | | |
| Carbinoxamine | ✓ | | |
| Chlorpheniramine | ✓ | | |
| Clemastine | ✓ | | |
| Cyproheptadine | ✓ | | |
| Dexbrompheniramine | ✓ | | |
| Dexchlorpheniramine | ✓ | | |
| Diphenhydramine | ✓ | | |
| Doxylamine | ✓ | | |
| Hydroxyzine | ✓ | | |
| Promethazine | ✓ | | |
| Triprolidine | ✓ | | |
| Antidiarrheal | | | |
| Diphenoxylate | | ✓ | |
| Antiparkinson | | | |
| Benzotropine (oral) | ✓ | | |
| Trihexyphenidyl | ✓ | | |
| Vasodilator | | | |
| Nylidrin | | ✓ | |
| Pentoxifylline | | ✓ | |
| Antispasmodic | | | |
| Belladonna alkaloids | ✓ | | |
| Clidinium–chlordiazepoxide | ✓ | | |
| Dicyclomine | ✓ | | |
| Hyoscyamine | ✓ | | |
| Propantheline | ✓ | | |
| Scopolamine 20 | ✓ | | |
| Stimulant | | | |
| Methylphenidate | | ✓ | |
| Antithrombotics | | | |
| Dipyridamole, oral short acting | ✓ | ✓ | ✓ |
| Ticlopidin | ✓ | | |
| Analgesic & anti-inflammatory | | | |
| Meperidine | ✓ | ✓ | ✓ |
| Aspirin >325 mg/d | ✓ | | |
| Diclofenac | ✓ | | |
| Diflunisal | ✓ | | |
| Etodolac | ✓ | | |
| Fenoprofen | ✓ | | |
| Ibuprofen | ✓ | | |
| Ketoprofen | ✓ | | |
| Meclofenamate | ✓ | | |
| Mefenamic acid | ✓ | ✓ | ✓ |
| Meloxicam | ✓ | | |
| Nabumetone | ✓ | | |
| Naproxen | ✓ | ✓ | ✓ |
| Oxaprozin | ✓ | ✓ | ✓ |
| Piroxicam | ✓ | ✓ | ✓ |
| Sulindac | ✓ | | |
| Tolmetin | ✓ | | |
| Indomethacin | ✓ | ✓ | ✓ |
| Ketorolac, includes parenteral | ✓ | ✓ | ✓ |
| Pentazocine | ✓ | ✓ | ✓ |

(Continued)

Table 1 (Continued)

| Drugs | Beers | McLeod | Beers and McLeod |
|-----------------------------------|-------|--------|------------------|
| Anti-infective | | | |
| Nitrofurantoin | ✓ | | |
| Cardiovascular | | | |
| α ₁ blockers | | | |
| Doxazosin | ✓ | | |
| Prazosin | ✓ | | |
| Terazosin | ✓ | | |
| α agonists, central | | | |
| Clonidine | ✓ | | |
| Guanabenz | ✓ | | |
| Guanfacine | ✓ | | |
| Methyldopa | ✓ | | |
| Reserpine (>0.1 mg/d) | ✓ | ✓ | ✓ |
| Antiarrhythmic | | | |
| Amiodarone | ✓ | | |
| Dofetilide | ✓ | | |
| Dronedarone | ✓ | | |
| Flecainide 35 | ✓ | | |
| Ibutilide | ✓ | | |
| Procainamide | ✓ | | |
| Propafenone | ✓ | | |
| Quinidine | ✓ | | |
| Sotalol | ✓ | | |
| Disopyramide | ✓ | ✓ | ✓ |
| Dronedarone | ✓ | | |
| Digoxin >0.125 mg/d | ✓ | | |
| Nifedipine, immediate release | ✓ | | |
| Spironolactone >25 mg/d | ✓ | | |
| Central nervous system | | | |
| Tertiary tricyclic antidepressant | | | |
| Amitriptyline | ✓ | ✓ | ✓ |
| Chlordiazepoxide–amitriptyline | ✓ | | |
| Clomipramine | ✓ | | |
| Doxepin >6 mg/d | ✓ | | |
| Imipramine | ✓ | ✓ | ✓ |
| Perphenazine–amitriptyline | ✓ | | |
| Trimipramine | ✓ | | |
| Antipsychotics | | | |
| Thioridazine | ✓ | | |
| Mesoridazine | ✓ | | |
| Barbiturates | ✓ | ✓ | ✓ |
| Amobarbital | ✓ | | |
| Butabarbital | ✓ | | |
| Butalbital | ✓ | | |
| Mephobarbital | ✓ | | |
| Pentobarbital | ✓ | | |
| Phenobarbital | ✓ | | |
| Secobarbital | ✓ | | |
| Benzodiazepines | ✓ | | |
| Alprazolam | ✓ | | |
| Estazolam | ✓ | | |
| Lorazepam | ✓ | | |

(Continued)

Table 1 (Continued)

| Drugs | Beers | McLeod | Beers and McLeod |
|--------------------------------------|-------|--------|------------------|
| Oxazepam | ✓ | | |
| Temazepam | ✓ | | |
| Triazolam | ✓ | ✓ | ✓ |
| Clorazepate | ✓ | | |
| Chlordiazepoxide | ✓ | ✓ | ✓ |
| Chlordiazepoxide–amitriptyline | ✓ | | |
| Clidinium–chlordiazepoxide | ✓ | | |
| Clonazepam | ✓ | | |
| Diazepam | ✓ | ✓ | ✓ |
| Flurazepam | ✓ | ✓ | ✓ |
| Quazepam | ✓ | | |
| Chloral hydrate | ✓ | | |
| Meprobamate | ✓ | | |
| Eszopiclone | ✓ | | |
| Zolpidem | ✓ | | |
| Zaleplon | ✓ | | |
| Ergot mesylates | ✓ | | |
| Isoxsuprine | ✓ | | |
| Skeletal muscle relaxants | | | |
| Carisoprodol | ✓ | ✓ | ✓ |
| Chlorzoxazone | ✓ | ✓ | ✓ |
| Cyclobenzaprine | ✓ | ✓ | ✓ |
| Metaxalone | ✓ | ✓ | ✓ |
| Methocarbamol | ✓ | ✓ | ✓ |
| Orphenadrine | ✓ | ✓ | ✓ |
| Endocrine | | | |
| Methyltestosterone | ✓ | | |
| Testosterone | ✓ | | |
| Desiccated thyroid | ✓ | | |
| Estrogens with or without progestins | ✓ | | |
| Growth hormone | ✓ | | |
| Insulin, sliding scale | ✓ | | |
| Megestrol | ✓ | | |
| Chlorpropamide | ✓ | | |
| Glyburide | ✓ | | |
| Gastrointestinal | | | |
| Metoclopramide | ✓ | | |
| Mineral oil, oral | ✓ | | |
| Trimethobenzamide | ✓ | | |

Note: American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2012;60(4):616–631, with permission from John Wiley and Sons.¹⁷ Reproduced with permission from McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *CMAJ.* 1997;156(3):385–391.¹⁸

Abbreviation: PIM, potentially inappropriate medication.

Results of the prevalence of PIM in this study can be seen in Table 3. We found that the overall prevalence of PIM was 52.2% (n=1,994) among the included records. Most of the PIM-prescribed medications are designated in the Beers criteria (75%). There are lists of drugs that were included

Table 2 General characteristics of subjects

| Characteristics | Distribution (%) |
|-----------------------|------------------|
| Age (years) | |
| 60–69 | 2,710 (71) |
| 70–79 | 958 (25) |
| ≥80 | 151 (4) |
| Sex | |
| Male | 1,632 (43) |
| Female | 2,187 (57) |
| Number of diseases | |
| 1 | 3,025 (79) |
| 2 | 744 (19) |
| ≥3 | 50 (1) |
| Number of medications | |
| 1–2 | 507 (13) |
| 3–4 | 3,104 (81) |
| ≥5 | 208 (5) |

in both the Beers and McLeod criteria, from which 24% of the PIM were prescribed. The most frequently prescribed PIMs were chlorpheniramine, mefenamic acid, ibuprofen, and nifedipine.

Meanwhile, as presented in Table 4, PIM prescription was not associated with age, sex, multiple diseases, and the use of ≤4 medications. Polypharmacy was an independent predictor of PIM, with an adjusted OR of 1.6 (1.2, 2.1), *P*-value =0.001. Furthermore, as can be seen in Table 5, the prevalence of PIM of patients receiving polypharmacy (5 or more drugs) was 63.5%, which was higher than those of nonpolypharmacy.

Discussion

In this study, we examined the prevalence of PIM among the Indonesian geriatric population in a primary care setting in the Karawang district. Its predictors were also determined to identify vulnerable groups prone to PIM and to better target intervention for reducing PIM. Assessment of PIM in primary care setting provides an overview of medication use pattern in the first point of contact with health professional. Appropriate initial treatment can prevent more serious complications among the elderly.²⁹

The use of PIM was highly prevalent among the study subjects (52.2%), implying the urgent need for improvement.

Table 3 Prevalence of PIM in Beers¹⁷ and McLeod¹⁸ criteria

| Criteria | Number of PIM (%) |
|------------------|-------------------|
| Beers | 1,505 (39.4) |
| McLeod | 17 (0.4) |
| Beers and McLeod | 472 (12.4) |
| Total | 1,944 (52.2) |

Abbreviation: PIM, potentially inappropriate medication.

Table 4 Results of logistic regression analysis

| Characteristics | OR (CI) | P-value |
|----------------------|----------------|---------|
| Age (years) | | |
| 60–69 | 0.9 (0.8, 1.1) | 0.661 |
| 70–79 | 1.0 (0.9, 1.2) | 0.578 |
| ≥80 | 0.9 (0.6, 1.3) | 0.829 |
| Sex | | |
| Male | 0.9 (0.8, 1.0) | 0.159 |
| Female | | Ref |
| Number of diseases | | |
| 1 | 0.9 (0.8, 1.1) | 0.668 |
| 2 | 1.0 (0.8, 1.2) | 0.778 |
| ≥3 | 1.1 (0.6, 2.0) | 0.620 |
| Number of medication | | |
| 0–4 medications | 0.9 (0.7, 1.3) | 0.927 |
| ≥5 medications | 1.6 (1.2, 2.1) | 0.001 |

Abbreviations: OR, odds ratio; Ref, reference.

Due to variabilities in the research setting, duration, and other criteria, a comparison with other studies was not straightforward. Despite these variations, we found that our results were comparable with previous findings. Slightly higher PIM was observed in studies conducted among the Japanese elderly in acute care, with a PIM prevalence of 56.1%,³⁰ and among elderly surgical patients in US hospitals (55.3%).³¹ On the other hand, a lower prevalence rate (32.2%) was observed in a study conducted in a UK primary care setting.³² Among other developing countries, the results of the current study were relatively much lower, for example, compared to those in Brazilian nursing homes (82.6%)³³ and in an Indian teaching hospital (87.3%).³⁴ The variations of these rates could be due to the differences in access to medicines, prescribing practices, and routine assessment of prescriptions by pharmacists.³⁵

In our study, the most frequently used PIM was chlorpheniramine, a first-generation antihistamine. It is strongly advised that this medication not be prescribed due to its high anticholinergic activity and increased risk of toxicity due to reduced clearance.¹⁷ Accidental deaths of the elderly under the influence of chlorpheniramine were reported in Japan.³⁶ Use of a second-generation antihistamine is recommended due to lower lipophilic properties, contributing to the prevention of the development of ADRs in the central nervous sys-

tem.³⁷ Certain nonselective nonsteroidal anti-inflammatory drugs (NSAIDs), such as mefenamic acid and ibuprofen, were also among the highly prescribed PIMs in the current study. Beers and McLeod criteria listed 19 NSAID drugs that should be avoided due to increased risks of gastrointestinal bleeding, renal failure, hypertension, central nervous system toxicity, and heart failure in the elderly.^{17,18} Acetaminophen and other NSAIDs with fewer side effects could be the safer alternatives for pain relief for a limited period in the elderly.³⁸

We found that polypharmacy (the use of ≥5 medicines) was relatively low among the study subjects (5%). Other studies have shown that polypharmacy among the elderly was in the range of 11.8%–45%.^{39–41} Despite the low prevalence in this study, polypharmacy was one of the strongest influential predictors of PIM use. Our finding is in agreement with previous reports.^{42–46}

Polypharmacy and its medical consequences has always been an issue for the geriatric population due to the need to treat the multiple illnesses that develop as patients age. However, to prevent unnecessary harm associated with polypharmacy, greater attention from health care professionals is needed. A thorough medication review for PIM and educational services for both patients and prescribers could be an option. The prescribing practices of physicians could be modified by familiarizing them with evidence from PIM criteria.^{47,48}

In this study, we found that multiple diseases were not associated with PIM. The variation in previous reports^{40,49} may be due to differences in disease characteristics and the availability of certain medicines for treating particular diseases in various regions included in PIM. In contrast with other studies,^{49,50} increases in age were not significantly associated with PIM, although a positive association was shown in the age group of 70–79 years old (OR: 1.0 [0.9, 1.2]).

Despite widespread utilization of Beers and McLeod criteria, one of the limitations of this instrument is its transferability to other region beside North America.⁵¹ It includes several drugs that are not available in Indonesian formularies or are rarely prescribed. However, since a medication appropriateness instrument is not yet available in Indonesia, we considered to use Beers and McLeods criteria to give initial overview on prescribing pattern in this region.

We realize that explicit tools like Beers and McLeod criteria cannot fully substitute comprehensive individual review of medications. These criteria only listed drugs in which the risk of use outweigh the benefit in elderly without paying attention on various aspect of treatment process, ie, indication.^{17,18} However, this type of criteria could give

Table 5 Relationship between number of drugs and prevalence of PIM

| Number of medication | n | PIM (%) |
|----------------------|-------|--------------|
| 1–2 | 507 | 223 (44) |
| 3–4 | 3,104 | 1,651 (53.2) |
| ≥5 | 208 | 132 (63.5) |
| Total | 3,819 | 2,006 (52.5) |

Abbreviation: PIM, potentially inappropriate medication.

advantages, including its straightforward application for large sample size and acceptable reliability, as opposed to implicit measures which rely on subjective clinical judgment of researchers.⁵²

The number of PIMs observed with the Beers criteria was higher than that observed with the McLeod criteria. Most drugs included in the McLeod criteria were included in the 2012 updated Beers criteria, indicating that the Beers set of criteria is an important prescribing assessment tool.^{17,18} However, the list may not always be suitable for implementation in all countries due to the different varieties of drugs registered and other prescribing practices. Therefore, there is a need to develop PIM criteria for specific countries.

This study, however, still has limitations. As only 25 primary health care facilities in Karawang District were involved, the generalizability of this result for the entire Indonesian geriatric population is limited. Furthermore, the association between the prevalence of PIM to ADR in patients receiving PIM was not assessed due to difficulties in collecting comprehensive patient medical data.

Conclusion

The prevalence of PIM in the current study was considerably high (55.2%), with polypharmacy found to be an independent predictor. Health care professionals are encouraged to review the medications prescribed for geriatric patients using updated safety guidelines to prevent the risks associated with PIM.

Disclosure

The authors report no conflicts of interest in this work.

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