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A REVIEW ON POTENTIALLY INAPPROPRIATE DRUG PRESCRIBING USING BEERS CRITERIA 2015

Introduction

The proportion of the elderly population has been gradually increasing over the last few years. The worldwide estimated number of elderly populations of 605 million in the year 2002 is expected to increase beyond 1.2 billion by 2025, with about 840 million representing developing countries.[1] Elderly people represent a population that requires special attention to their drug usage. This group is characterized by pluripathology, functional and cognitive impairment and physiological changes developing with age, which modify the pharmacodynamics and pharmacokinetics of drugs.[2] This leads to a complex medication usage process among elderly patients and render additional chances of potentially inappropriate medication.[3]

Inappropriate medications are defined as medications in which the risk outweighs the benefit. The risk/benefit ratios of some medications are unfavorably affected by age-related changes in the medications pharmacokinetic and pharmacodynamic parameters in older persons. Prescribing of the inappropriate agents in an elderly population thereby exposes the patients to a greater risk of drug-related morbidity and mortality. Therefore, it is important to identify inappropriate medication usage among current prescribing patterns and to improve future prescribing patterns.[4]

Several guidelines were developed for identifying and reducing drug-related problems, improving medication prescription safety, and medication selection among the elderly. Among them Beers criteria is the most widely accepted and commonly used.[4] Beers criteria was first developed in 1991 to provide guidance on PIM use and helped to create a consistent and explicit measure of inappropriate medication use among the elderly.[5] The criteria in the list are not all absolute contraindications; furthermore, there are situations in which the use of medications included in the criteria can be appropriate. This review chose studies examining the 2015 Beers criteria because the updated 2015 version is more specific to improve the quality of medication use among older patients. The changes in the 2015 update include addition of two key components: drug dose adjustment required based on kidney function, and Drug-Drug Interactions(DDI).[6]

The following is a review of the literature applying the 2015 criteria for inappropriate medication use in the elderly developed by Beers to prescribing practices in various healthcare settings.[6]

Findings

This review has considered ten studies which applied the Beers criteria to examine inappropriate medication use among the elderly patients in various healthcare settings. These included primary healthcare centers, community pharmacies, assisted living facilities, teaching hospitals, housing hospitals

and outpatient departments.

Table 1 gives the details of the studies examining inappropriate medication use by the elderly patients using Beers criteria. All studies involved patients aged above 65 years of age except the study performed by Saka SA et al., (2018) which considered patients aged above 60 years. [7]

Each study was reviewed for prevalence, nature and extent of inappropriate medication use, and factors associated with their use. Prevalence of potentially inappropriate medications was a common issue among all the studies except the study performed by Yoon SJ et al., (2018) which investigated the status of potentially harmful drug–drug interactions in elderly patients as per BC 2015.[8]

Another study conducted by Chun JC et al., (2018) among a frail population in assisted living facilities assessed the relationship between the potentially inappropriate medication usage and their effect on falls and hospitalizations.[9] Saka SA et al., (2018) conducted a study among Nigerian and South African elderly patients to determine the association between the PIM usage and ADRs.[7] Kose E et al., (2018) performed a study to establish whether the PIM usage affects the nutritional status among elderly patients.[10]

Table 1. Studies Examining Inappropriate Use of Medications by the Elderly Using the Beers Criteria

S. No	Study	Setting	Scope (sample size)	Study Design	Data sources (year of data collection)	Prevalence	Criteria
1	Bazargan M et al., (2018)	Senior housing units	South Los Angeles (193)	Cross-sectional Observational	Medical records (November 2015 – February 2017)	46%	Updated Beers criteria 2015
2	Chiapella LC et al., (2018)	Primary healthcare centre and Community Pharmacy	Argentina (2368 in community pharmacy (CP) and 263 in Primary healthcare centre (PHC)	Cross-sectional Observational study	Prescriptions (February and April 2015)	In CP 4.69% And in PHC 8.13%	Updated Beers criteria 2015
3	Khamis S et al., (2019)	University Hospital	Northern Cyprus (119)	Cross-sectional Prospective	Review of case sheets (September and October 2016)	16.9% during admission and 12 % during discharge	Updated Beers criteria 2015

4	Saka SA et al., (2018)	Teaching Hospital	Nigeria (268) and South Africa (339)	Cross-sectional Retrospective	Patient drug chart (13th April to 25th November 2017.)	Nigeria (32.1%) and South Africa (30.1%)	Updated Beers criteria 2015
5	Chun JC et al., (2018)	Assisted Living facilities	North Virginia (132)	Retrospective Observation	Patient Drug Chart review (January2016 to October 2017)	60%	Updated Beers criteria 2015
6	Kose E et al., (2018)	General Hospital	Ibaraki, Japan (929)	Retrospective longitudinal Cohort study	Medical records at admission and discharge (July 2010 and March 2016)	37% during admission which is decreased to 31% during discharge	Updated Beers criteria 2015
7	Bo M et al., (2017)	Two tertiary care hospitals	Northern Italy (1000)	Prospective cohort Observational	Direct interview and interview of clinical records (2015-2016)	63%	Updated Beers criteria 2015
8	Patel R et al., (2018)	Thirteen mobile Medicare centres	Northern and Central California (703)	Cross-sectional Interventional study	Patients medical records (October 15 to November 21, 2015)	29%	Updated Beers criteria 2015
9	Al-azayzih A et al., (2019)	University Hospital	Jordan (4622)	Cross-sectional Observational study.	Patient case sheets (October to the end of December 2016)	62.5%	Updated Beers criteria 2015
10	Yoon SJ et al., (2018)	University Hospital	Korea (1, 257 317)	Observational	Insurance claims data from the Health Insurance Review and Assessment Service (January to December 2016)	-	Updated Beers criteria 2015

Prevalence of Inappropriate Medication Use

Prevalence is defined as the percentage of patients using inappropriate medications.[4] Prevalence ranged from 4.69%[2] in Community Pharmacies to 63%[11] among tertiary care hospitals. The reason for the high prevalence among tertiary care hospitals is because of the prolonged hospitalization and the studies were conducted for a longer duration. The lower prevalence rate in the community pharmacy is because of limited polypharmacy. The variation in prevalence rate may be due to the length of hospitalization, type of healthcare setting and duration of the study performed.

Studies involving prevalence rates of greater than 20% incorporated tertiary care hospitals, assisted living facilities, teaching hospitals and senior housing hospitals. This indicates that inpatients with the prolonged hospitalization have a higher prevalence of PIM use than outpatients. The study performed by Khamis S et al., (2019) compared the prevalence rates of PIM usage among inpatients and outpatients and showed a higher prevalence rates among inpatients 16.9% than outpatients 12%.[5]

Among all the studies the study performed by Khamis S et al., (2019) considered all four categories of the updated BC 2015 and the prevalence rates are as follows. The Prevalence of PIM as per the second category in BC that may exacerbate the disease or syndrome was 22%. Furthermore, the prevalence of 19.4% of PIMs was found for drugs that are to be used with caution in elderly patients. For the drugs which are to be used with caution among the patients suffering from kidney impairment showed a prevalence of 7.1% during admission and 3.1% during discharge.[5]

Nature of Inappropriate Medication Use

This review revealed that mostly one potentially inappropriate medication per patient was observed among all the studies. The study performed by Khamis Set al., (2018) showed an equal percentage of one and two PIM use.[9] The percentage of two inappropriate medication usage ranged from 13%[12] in senior housing units to 30.5%[5] in university hospital.

The most commonly prescribed inappropriate medications observed among the studies were Proton Pump Inhibitors 67%, cardiovascular agents 56%, Pain relieving medications 45% like NSAID's and Opioid analgesics, CNS agents 45% like Benzodiazepines, Hypnotics, and Anti Psychotics. The second category of BC include Drug -Disease interactions and 52.6% of drugs were found to interact with delirium whereas 3.9% of the drugs were found to interact with history of fall and history of syncope. Drugs to be used with caution included Antipsychotic medications, Diuretics and Mirtazapine.[5]

The study performed by Al-azayzih A et al., (2019) conducted the third category of Beers Criteria that are drugs to be used with caution and these included Diuretics 45.1%, Aspirin for primary prevention of cardiac events among older adults aged ≥80 years 38.8%, and vasodilators 12.3%.[13]

Drug-Drug interactions that are to be avoided in the elderly are included in the 2015 update. These include interactions resulted from the simultaneous prescribing of at least two different medications with Anticholinergic properties like first-generation Antihistamines (Chlorpheniramine and Triprolidine), Antimuscarinic medications (Oxybutynin) and Antispasmodics (Clidinium-Chlordiazepoxide and Hyoscyamine).[13] Drugs to be avoided or have their dosage adjusted based on varying levels of kidney function in older adults included use of Gabapentin when CrCl <60 ml/min.[13]

Factors Associated with Inappropriate Medication Use

Various factors associated with PIM use are listed in Table 2. Factors associated with inappropriate medication use varied from study to study. Most studies reported higher rates of PIM usage in patients with polypharmacy. Three studies conducted by Khamis S et al., (2019), Chun JC et al., (2018) and Kose E et al., (2018) reported a higher rate of PIM prescribing among the patients with prolonged hospitalization.[5,9,10] Studies conducted by Khamis S et al., (2019) and Bazargan M et al., (2019) found a higher rate of PIM use in patients with chronic conditions and hospitalization associated mental disorders.[5,12] Other associated factors with PIM use include Sex of the patient (women were more prone to PIM use) and Race (Whites were more prone to the use of PIM). In patients with low-income beneficiaries also found a great range of PIM use.

Table 2. Selected Findings of the Studies Examining Inappropriate Use of Medications by the Elderly Patients in Various Settings

S. No	Study	Prevalence • One medication • ≥ Two medication	Frequently prescribed inappropriate medication	Factors associated with PIM use
1	Bo M et al., (2017)	29.6% of one PIM use 19.8% of two PIM use	Antipsychotics, Hypnotics, PPIs and Digoxin dosage >0.125 mg/daily	1.Psychiatric behavioural disorders (including dementia) 2.Intermediate- to long-term care discharge 3.No. of medications before admission 4.No. of medications at discharge
2	Chiapella LC et al., (2018)	-	Glibenclamide, Ibuprofen, Digoxin, Diclofenac, Amiodarone, Meloxicam	1. Sex of the patient 2. No. of drugs used
3	Chun JC et al., (2018)	22.1 % of one PIM use 22.1% of two PIM use	CNS medications, Gastrointestinal agents, pain medications, Anticholinergic drugs, Endocrine, and Cardiovascular medications.	-
4	Saka SA et al., (2018)	32.1% of one PIM use in Nigeria 30.1% of one PIM	Cardiovascular agents, Anti-	1.psycho analeptic medications as associated factors for ADRs in Nigeria

		use in South Africa	inflammatory, Anti-rheumatic, NSAIDs and Opioids	
5	Bazargan M et al., (2018)	26% of one PIM use 13% of two PIM use	PPIs and CNS active agents	1. Higher number of medications 2.Higher number of chronic conditions 3.Six chronic conditions
6	Khamis S et al., (2019)	36.6% of one PIM use 30.5% of two PIM use	PPIs like Pantoprazole Diuretics such as Furosemide, Low molecular weight Heparin like Enoxaparin	1.Polypharmacy 2.Hospitalization
7	Kose E et al., (2018)	37% of one PIM use 15% of two PIM use	First-generation Antihistamine, Antipsychotic, Benzodiazepine, PPIs and NSAIDs	1.Poor resistance to disease and vulnerability to stressful factors in elderly patients 2.Long-term hospitalization can induce mental disorders
8	Patel R et al., (2018)	29% of one PIM use	Alprazolam, NSAIDs, like Naproxen, Conjugated Estrogen vaginal cream, Zolpidem, Amitriptyline.	1.Whites 2.Women 3. Low-income beneficiaries.
9	Al-azayzih A et al., (2019)	39.6% of one PIM use 23.3% of two PIM use	Pain medications, gastrointestinal medications, and Antispasmodics.	1.Female gender 2.Polypharamcy
10	Yoon SJ et al., (2018)	-	Corticosteroids, NSAIDs, combination of two or more Anticholinergic drugs and three or more drugs acting on the CNS	1.Female patients 2.Medical aid beneficiaries 3.Patients using multiple healthcare institutions 4.Frequent outpatient visitors 5.Patients prescribed more than six medications in a single prescription

Outcomes Associated with Inappropriate Medication Use

Various adverse outcomes were associated with PIM use which decreases the quality of life

among elderly patients. Use of Insulin sliding scale among heart failure patients, prescription of Digoxin ≥0.125 mg/day and Antipsychotics were associated with higher risk of mortality and rehospitalization within 6 months of such usage.[11]

Chun JC et al., (2019) conducted a study to assess the relationship between PIM usage and their effect on falls and hospitalization in a frail population revealed that there was no statistical significance between PIM usage and fall rates but there was a positive correlation between PIM usage and hospitalisations.[9]

A positive correlation was found between PIM usage and occurrence of ADRs among elderly patients in the study performed by Saka SA et al., (2018).[7] PIMs were responsible for 34.9% and 32.3% ADR cases in Nigeria and South Africa respectively.[7] About 56% of falls and fall-associated bone fractures were associated with PIM usage among elderly patients.[12] The PIM usage was independently and negatively correlated with Geriatric Nutritional Risk Index at discharge.[10]

This review suggests that inappropriate medical use was associated with various drug-related problems which decrease the quality of life among elderly patients.

Discussion

In order to improve the prescribing patterns, current drug utilization should be understood. This review helps in understanding the inappropriate drug use among elderly patients using Beers criteria. Issues examined in this review included prevalence, nature and extent of PIM use and factors associated with such usage. All 10 studies considered for the review applied the Beers criteria 2015 but only applied the first category of BC that is drugs

that are to be avoided in the elderly based on organ system classification. Only one study conducted by Khamis S et al., (2019) included all the four categories of BC 2015.[5] Most researchers did not apply the Drug-Drug Interactions, Drug-Disease Interactions and drugs to be used with caution among the patients with an impaired renal function that is to be avoided among the elderly patient as per BC 2015.

Prevalence of inappropriate drug use ranged from 4.69%[2] in community pharmacies to 63%[11] among tertiary care hospitals and most common drugs include Proton pump Inhibitors, Pain relieving medications, Cardiovascular drugs and CNS agents. These results suggest that a pharmacist review to decrease inappropriate prescribing should focus on the mentioned medications.

Various factors were associated with inappropriate drug usage. Polypharmacy was a common factor among the studies performed by Chiapella LC et al., (2018), Khamis S et al., (2018) , Bazargan M et al., (2018) and Al-azayzih A et al.,(2019).[2,5,12,13] Prolonged hospitalization in case of chronic disease condition was the next common factor observed among the studies performed by Chiapella LC et al., (2018) and Kose E et al., (2018).[2,10] Sex of the patient was a common factor among two studies performed by Al-azayzih A et al., (2019) and Patel R et al., (2018).[13,14] Since these factors were observed among most studies these factors serve as an important marker for inappropriate drug use among elderly patients. These factors can be incorporated into drug use control systems in healthcare. Also, many studies conducted the risk of ADRs and falls in relation to the PIM use. A positive correlation was found among PIM usage and ADRs in the study performed by Saka SA et al., (2018).[7] Bazargan M et al., (2018) found that 56% of falls and fall-associated bone fractures were

associated with PIM usage among elderly patients .[12]

Future studies should address these issues in examining the overall impact of inappropriate prescribing on the quality of life among elderly patients.

Summary

This review revealed some consistent patterns across healthcare settings. Issues examined in this review included prevalence, nature and extent of PIM use and factors associated with the use of inappropriate medications.

Studies using patient-based prevalence showed that between nearly one in four and one in seven elderly patients received an inappropriate medication. These medications include PPIs, Pain relieving medications like NSAIDs and Opioid analgesics, cardiovascular agents, CNS medications like Benzodiazepines, Hypnotics, and Anti Psychotics. Antipsychotic medications, Diuretics and Mirtazapine were observed as the drugs to be used with caution among elderly patients.

Certain factors were outlined for inappropriate medication use and these include women, patients >80years of age, and Medicaid patients. Several studies reported a positive association between the number of medications and inappropriate prescribing.

Various adverse outcomes like rehospitalization, increased risk of falls, ADRs and increased cost of living were resulted with PIM use. In India, the population of elderly patients is increasing rapidly and there is a need to use Beers criteria effectively to identify and avoid inappropriate drug usage.

This review can be useful in developing targeted interventions to influence future drug usage among the elderly. Further research is required to identify and address the impact of potentially inappropriate medication use among the elderly in India. This study not only helps in identifying the inappropriate drug use but also helps guide in the further update of Beers criteria.

Acknowledgement

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Appendices

Abbreviation	Full form
ADR's	Adverse Drug Reactions
BC	Beers criteria
CNS	Central Nervous System
CP	community pharmacy
DDI	Drug-Drug Interaction
NSAID's	Non-Steroidal Anti-inflammatory Drugs
PHC	Primary healthcare centre
PIM	Potentially Inappropriate Medication