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Determinants of potentially inappropriate medication in elderly: A hospital based cross sectional study

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ABSTRACT

Background: Inappropriate prescribing in the elderly is considered as a major public health issue. Identification of factors associated with the occurrence of potentially inappropriate medications (PIMs) in elderly is essential to reduce the morbidity, healthcare expenditure, decreased quality of life and adverse drug reactions.

Objectives: To find out the prevalence and the determinants of PIMs using the American Geriatric Society (AGS) Beers Criteria of 2015.

Methods: The cross-sectional study was carried out on 800 elderly patients who were 65 years or more, attending the out-patients departments (O.P.Ds) of a tertiary care hospital in Odisha (a state in eastern India). Descriptive statistics were used to report the prevalence and pattern of PIMs. Chi-square analysis with Fisher's exact when appropriate was used to find out the association between the categories of drugs used in the prescriptions and the PIMs. Bivariate analysis followed by multivariate logistic regression analysis was used to evaluate whether age, gender, co-morbidity and number of medications (poly-pharmacy) could be the determinants of PIM in elderly.

Results: PIMs were received by 21.87% patients. Patients in the age group of 65-74 years received maximum number of PIMs. Poly-pharmacy was a significant determinant of inappropriate medication (adjusted OR: 1.95, 95% CI: 1.19 - 3.01).

Conclusions: Inappropriate prescribing in elderly patients is common. Increased number of concurrent medications use was a significant determinant of inappropriate medication. There is a need for rational drug therapy in elderly patients to prevent the occurrence of potentially inappropriate medications.

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INTRODUCTION

Inappropriate prescribing in the elderly population is a major public health issue because of its direct association to morbidity, mortality and wastage of health resources. Worldwide up to 30% of hospital admissions in elderly are related to adverse drug events.¹ Older people often experience multiple co-morbidities and are prescribed multiple medications thereby increasing the risk of adverse drug events and drug interactions due to the associated patho-physiological complexity.^{2,3} Age-related physiological changes alter the pharmacokinetics and pharmacodynamics.⁴ As a result of these changes some drugs like benzodiazepines, non-steroidal anti-inflammatory drugs pose special risks to older people.^{5,6} Prescription of such drugs are inappropriate, particularly where safer alternatives exist. Hence, screening of potentially inappropriate medications (PIMs) appears compelling. Several explicit and implicit criteria-based prescribing tools e.g. Beers criteria, Inappropriate Prescribing in the Elderly Tool (IPET), Screening Tool of Older Persons' potentially inappropriate

Prescriptions (STOPP) have been devised using expert reviews and opinions to identify PIMs in the elderly. Among these, Beers criteria are the most widely referred tool internationally because of their high reliability and reproducibility.⁷

Over the past century, life expectancy has increased dramatically. Between 2000 and 2050, the number of older adults worldwide is expected to increase from 420 to 974 million.⁸ In India, the elderly population is expected to reach over 316 million by 2050.⁹ In the U.S., elderly age group comprise 12% of the population and receive 30% of all prescriptions.¹⁰ This social transformation represents a challenge to provide appropriate, affordable and accessible health service to this vulnerable age group.

The management of therapy in elderly is a critical aspect of all levels of health care. Published literature related to the epidemiology of potentially inappropriate medication use in elderly in this part of the country is limited. Identification of factors associated with the occurrence of PIMs in elderly is essential to reduce the morbidity and mortality, increased cost, decreased quality of life and

adverse drug reactions associated with PIMs. Elsewhere studies on PIM in elderly have been either community based or have focused on a particular group of patients and have used the older version of Beers criteria.⁷ None of the existing studies on PIM in elderly have used the out-patient department as a study setting. In the present study the out patients department was chosen to find out the potentially inappropriate medications in elderly because, in this setting the interaction between the patient and the treating physician is very brief and the chances of PIMs are higher. With this background, the study was carried out with the objective to find out the prevalence and the determinants of potentially inappropriate medications in elderly in the out-patient department of a tertiary care hospital using the American Geriatric Society (AGS) Beers criteria of 2015.

METHODS

Study Design and Setting

It was a hospital based cross sectional study, conducted in Maharaja Krishna Chandra Gajapati (M.K.C.G.) Medical College and Hospital, a 1200 bedded tertiary care teaching hospital in Eastern India, in the state of Odisha from February 2016 to May 2016. Drug dispensing in this hospital is through the hospital formulary as well as the private retail pharmacy outlets set up in the out-patient department (O.P.D) annex. The drugs available in the hospital formulary are procured on the basis of the National List of Essential Medicines recommended by Central Drugs Standard Control Organization, Department of Health and Family Welfare, Government of India.

Sample Size Calculation and Sampling Technique

The source population was elderly patients aged 65 years and more. Assuming the prevalence of PIM to be 20%, an absolute precision of 3, a desired confidence level of 95% and assuming the response rate of 85%, the sample size was calculated to be 786 using nMaster 2.0, (Designed and Developed by Department of Biostatistics, Christian Medical College, Vellore, India). Finally, 800 patients of both gender who were 65 years or more, and attending the out-patients departments of general medicine, surgery, gynaecology, orthopaedics, psychiatry, skin, pulmonary medicine, ophthalmology, ENT, oncology and dentistry were included in the study. The O.P.Ds selected to enroll the study participants were based on the information that, during the year prior to the initiation of this study, majority of elderly population in the O.P.D belonged to these departments. So, these O.P.Ds were included in the study to avoid selection bias. Convenience sampling technique was adapted to include the participants who met the inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

All patients new as well as old of either gender who had completed 65 years of age as on 31st January 2015 were included in the study, whereas patients unable to

communicate, seriously ill, requiring ICU admission, on palliative care or unwilling to participate and those having incomplete information were excluded from the study.

Data Collection

The data was collected by the investigators. A time period of seven days in a sequential manner was spent in each of the selected O.P.Ds. All the participants were interviewed only once and their prescriptions were checked individually for the necessary information to fill up the case record forms. For the purpose of the study a 'prescription' was defined as a single order by a prescriber and not the full medication profile of patient at a time.

Study Instrument

The data was collected in a structured and pre-tested case record form. The design of the case record form was guided by the American Geriatric Society Beers criteria of 2015 to identify the potentially inappropriate prescriptions in elderly. Beers criteria were first described in 1991 and subsequently updated in 1997, 2003, 2012 and 2015.¹¹ In 2012 and 2015, the Beers criteria were updated with the partnership of the American Geriatrics Society (AGS) for regular, transparent, systematic updates and support for the extensive use of the criteria by clinicians for their use in research, policy, and practice.¹² AGS Beers criteria of 2015 is a comprehensive set of explicit criteria that gives status to a drug as appropriate or inappropriate for the elderly aged 65 years and above in given conditions. The AGS Beers criteria of 2015 identifies PIMs based on five components – according to organ system, therapeutic category and drug, according to disease or syndrome, according to drugs to be used with caution, according to drug interactions and according to renal function.¹³ In the present study, a 'prescription was considered to be inappropriate if it contained one or more drugs included in any of the components of AGS Beers criteria of 2015'. Identification of the PIMs according to renal function required the estimation of creatinine clearance of all the study participants. The creatinine clearance was estimated indirectly using Cockcroft-Gault equation [Creatinine Clearance = (140-Age in years) x Weight in kg/ (72 x Serum Creatinine in mg/dl)].^{14, 15}

Data Processing and Analysis

The data collected in the structured case record form were entered and analyzed using SPSS version 16.0 (copyright SPSS Inc. 2007, Chicago, IL, USA). Besides, the data were checked and cleaned for their completeness and errors in data entering. Descriptive statistics were used to report the prevalence and pattern of PIMs. Chi-square analysis with Fisher's exact when appropriate was used to find out the association between the categories of drugs used in the prescriptions and the PIMs. Bivariate analysis followed by multivariate logistic regression analysis was used to evaluate whether age, gender, co-morbidity and number of medications (poly-pharmacy) could be the determinants of PIM in elderly.

Ethical Consideration

Ethical clearance was obtained from the Institutional Ethics Committee of M.K.C.G. Medical College, Berhampur, Odisha. All the eligible participants in the study were explained clearly about the purpose and nature of the study in the local language (odia) or in any other language they could understand. Written informed consent was obtained before including them in the study.

RESULTS

Out of the 800 patients, 484 (60.5%) were males and 316 (39.5%) were females. The average age of the patients was 75.8 ± 6.9 years, the age range being 65 - 85 years. The average diagnosis per patient was found to be 2.55 ± 0.81. Most of the patients presented with an acute medical problem on a background of chronic illness. 112 (14%) patient were diagnosed to have one disease followed by 385 (48.12%) patients were having two diseases and 303 (37.87%) patients were found to have three or more diseases.

Each patient, on an average, was taking prescriptions for 7.17± 1.29 medications at the point of data collection. The total numbers of drugs prescribed were 6776 in 800 prescriptions. On the category-wise distribution of the prescribed drugs, it was found that CVS drugs were the most frequently prescribed drugs (18.59%) followed by vitamins and mineral supplements, and drugs for endocrine diseases. Out of the 6776 drugs prescribed, 339 were inappropriate (5%) as per AGS Beers criteria 2015. Analgesics constituted commonest PIMs (26.25%) followed by drugs for CNS (17.99%). There was a significant association between the type of drug prescribed and the occurrence of PIM except in the drugs prescribed to treat cardiovascular, endocrine and genitourinary diseases (Table 1). About 48% of the drugs dispensed through the hospital

Table 1. Category of drugs prescribed inappropriately in elderly as per AGS Beers criteria of 2015

Drug category	No. of medications (%) N = 6776	No. of PIMs (%) n = 339	Fisher's exact test p value
Cardiovascular drugs	1260 (18.59)	54 (15.92)	0.223
Vitamins and dietary supplements	1220 (18.00)	0 (0)	< 0.001
Endocrine drugs	1052 (15.52)	46 (13.57)	0.355
Gastro-intestinal drugs	835 (12.32)	14 (4.12)	< 0.001
Respiratory drugs	715 (10.55)	0 (0)	< 0.001
Analgesics	550 (8.11)	89 (26.25)	< 0.001
Minerals	412 (6.08)	0 (0)	< 0.001
Anti-infective	255 (3.76)	48 (14.15)	< 0.001
Central nervous system drugs	158 (2.33)	61 (17.99)	< 0.001
Genitourinary drugs	134 (1.97)	7 (2.06)	0.84
Miscellaneous	185 (2.73)	20 (5.89)	< 0.001

Miscellaneous includes drug categories like anti-histaminics, anti-spasmodics, oral anticoagulants, drugs to treat hyperuricemia

Table 2. Number of drugs prescribed inappropriately in elderly as per different components of AGS Beers criteria of 2015

Component of AGS Beers Criteria of 2015	Number of drugs (%)	p value (95% CI)
According to organ system, therapeutic category	213(62.83)	< 0.0001 (57.44-67.99)
According to disease or syndrome	51(15.04)	< 0.0001 (11.42-19.31)
According to drugs to be used with caution	32(9.44)	< 0.0001 (6.55-13.06)
According to drug interactions	24(7.08)	< 0.0001 (4.59-10.35)
According to renal function	19(5.60)	< 0.0001 (3.4-8.61)

formulary were common to AGS Beers criteria of 2015, whereas all the drugs enlisted in the Beers criteria were available in the private retail pharmacy outlets in the O.P.D annex.

At least one PIMs was received by 175 (21.87%) patients. 122 prescriptions had one PIM, 41 had two and 12 had three or more PIMs concurrently. The study recorded 240 PIMs in 800 prescriptions (30%). According to the categories of inappropriate prescribing as per AGS Beers Criteria 2015, majority of the PIMs belonged to the category identifying potentially inappropriate medications according to organ system, therapeutic category (62.83%, 95% CI 57.44 - 67.99) followed by PIMs according to disease or syndrome (15.04%, 95% CI 11.42 - 19.31) (Table 2).

Table 3. Predictors of potentially inappropriate medication in elderly as per AGS Beers criteria of 2015

Patient characteristics	Number of patients (N=800)	Number of patients with PIM (n=175)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Gender				
Male	484	109	1.10 (0.78-1.55)	1.5 (0.87-1.91)
Female	316	66		
Age (in years)				
<75	376	108	0.82 (0.58-1.16)	1.68 (0.92 - 3.04)
>75	424	67		
Number of medications (poly-pharmacy)				
<5	468	38	7.95 (5.34-11.82)*	1.95 (1.19-3.01)*
>5	332	137		
Number of diseases (co-morbidity)				
1-2	497	99	1.34 (0.95-1.89)	2.37 (0.96-1.64)
>2	303	76		

PIM: Potentially inappropriate medication. *Statistically significant at p < 0.05

The prevalence of PIMs in elderly patients less than 75 years was higher (29%). It was observed that 42% of patients were prescribed with more than 5 drugs. 303 (37.87%) patients had more than two co-existing diseases. These patients had a higher prevalence of inappropriate medications. Using logistic regression analysis, it was identified that increased number (>5) of concurrent medications use (adjusted OR: 1.95, CI: 1.19 – 3.01, P < 0.01) was a significant determinant of inappropriate medication. Though male gender, an age less than 75 years and a larger number of co-morbid conditions increased a likelihood of PIM but the observations were statistically not significant (Table 3).

DISCUSSION

As per AGS Beers criteria of 2015, the prevalence of potentially inappropriate medications in the present study was 21.87%. Many other studies have reported the prevalence of inappropriate medication in elderly using the older versions of Beers criteria. In a study done in Korea, they have reported the prevalence to be 58.2%.¹⁷ Similar studies done in India have reported a prevalence of 23%.^{18,19} A study done in France has reported the prevalence to be 66%.²⁰ The wide variability in the prevalence of PIMs reported in various studies may be due to the differences in study setting, disease characteristics, prescribing patterns and criteria adopted to identify the PIMs. A geographical variation among physicians' awareness of regarding the existence of a list of inappropriate drugs for the elderly may have led to differences in prevalence of PIM. In the present study at least one PIM was observed in 22.52% males and 20.88% females. A study done in the west has reported a higher prevalence of PIM in elderly females (31%) than in males (26%).²¹

It was observed in the present study that the most frequently prescribed class of PIMs were analgesics followed by drugs for central nervous system ailments. Whereas, a study done in Karachi, Pakistan, has reported that central nervous system drugs (58.7%) followed by anti-cholinergics (21.2%), and cardiovascular medications (10.8%) were the frequently prescribed PIMs.²²

In the present study it was observed that poly-pharmacy with more than five drugs was a significant determinant of potentially inappropriate medication in elderly. Often, therapy in elderly is for multiple disease conditions with multiple drugs, so this observation has sufficient clinical relevance. In a study done in Singapore where poly pharmacy was observed in 58.59% of the participants, the prevalence of PIMs was 70%.²³ Poly-pharmacy not only increases the adverse drug events but also rises the cost of treatment. In a prospective cohort study done in Karachi, they have reported a higher prevalence of adverse drug reaction in elderly patients who were on poly-pharmacy.²² In another study done in Northwestern University, it has been observed that, as the number of diagnosis increases, the number of medications to treat each particular disease condition also increases and this leads to inappropriate medications.²⁴

Many studies done in India and elsewhere have

associated age, gender, multiple medications, and co-morbidity with increased risk of PIM.^{23,24,25} Similar were the observations in this study where age, gender, co-morbidity increased the likelihood of PIM but they were not statistically significant determinants of inappropriate prescribing in elderly. This could be due to the fact that, many of the medications used to treat some of the diseases in the study population were not included as inappropriate in AGS Beers Criteria of 2015, leading to a lower reporting of the occurrence of the PIM in the study population.²⁶

There are some limitations of the present study. Being an O.P.D based study; it does not describe the prevalence of the PIMs in the in-patient departments. This study has been conducted in a hospital setting, so it does not describe the situation in the community. Moreover, though AGS Beers criteria of 2015 are widely accepted to evaluate PIMs in elderly, its suitability for Indian hospital O.P.D setting has not yet been adequately explored by a large number of published literatures. Still, this was adapted as a study tool due to non-availability of an Indian guideline with respect to the geriatric population in the country. Further, in the present study, a prescription was considered to be inappropriate if it contained one or more drugs included in any of the five components of AGS Beers criteria of 2015. This might have overestimated the prevalence of PIMs, as some PIMs may be disease or dose specific. The exclusion of seriously ill, patients requiring ICU admission, patients on palliative care is another limitation of this study.

CONCLUSIONS

Increased number of concurrent medications use was a significant determinant of inappropriate medication. The findings of this study imply that special care must be adopted in elderly who are being treated with multiple drugs for co-morbid conditions. There is a need for rational drug therapy in elderly to avoid poly-pharmacy as it increases the risk of occurrence of potentially inappropriate medications.

CONFLICTS OF INTEREST STATEMENT

No conflict of interest was declared among authors.

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