

## Comparison of Beers criteria and EU(7) potentially inappropriate medications list for the potentially inappropriate medications in Indian elderly inpatients

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### ABSTRACT

**Background:** Use of inappropriate medication is an important problem in present geriatric clinical practice. No specific potentially inappropriate medications (PIM) tools are available considering the availability of drugs in India. Aim and objective were to assess prevalence and pattern of potentially inappropriate medication (PIM) use in elderly inpatients by updated Beers criteria 2015 and EU(7) PIM list 2015.

**Methods:** This cross-sectional study was carried out on medical records of elderly patients ( $\geq 65$  yrs) admitted in the internal medicine wards and intensive care units (ICU) over a period of 6 weeks. The medications were evaluated for the PIM use as per Beers criteria and EU(7) PIM list.

**Results:** A total of 225 patients (mean age- 71.48 yrs) were admitted in internal medicine wards and ICU during study period. Total 184 PIM belonged to 33 different medications were used during study period. The prevalence of PIM in internal medicine wards and ICUs were 51.96% and 57.14%, respectively. The prevalence of PIM was significantly higher with the EU(7) PIM list than Beers criteria (49.77% vs. 21.77%) [ $p < 0.0001$ ]. The commonly prescribed PIM were dextromethorphan (13.33%), ranitidine (11.11%) and glipizide (10.22%).

**Conclusions:** Elderly patients frequently receive PIM. EU(7) PIM list identifies more PIM among elderly inpatients than Beers criteria.

**Keywords:** Beers criteria, EU(7) PIM list, Elderly, Internal medicine wards, Intensive care units, Potentially inappropriate medications

### INTRODUCTION

An elderly person receives more drugs than other age groups due to multiple comorbidities. Moreover, age related pharmacokinetic and pharmacodynamic changes prone them for the adverse drug reactions.<sup>1</sup> Earlier systematic reviews observed elderly patients are at high risk of having adverse drug reactions.<sup>2,3</sup> An inappropriate medication prescribed is the major problem in present clinical practices.<sup>4</sup> A potentially inappropriate medication (PIM) refers to prescription of drugs carrying risks outweighing the expected clinical benefits, especially

when there is evidence for an equally or more effective and safer alternative medication.<sup>4</sup> The use of PIM is associated with the risk of adverse drug reactions and adverse drug events.<sup>5,6</sup> An earlier systematic review observed the use of PIM is associated with higher rates of hospitalisation, health care costs and quality of life problems.<sup>7</sup> It is important to identify and reduce the PIM use in an elderly population.

There are various tools available to evaluate PIM use in an elderly population.<sup>8-11</sup> The Beers criteria have been widely used to identify and monitor PIM use in elderly patients in

internal medicine wards and ICU hospitalisation.<sup>12-20</sup> The Beers criteria have been updated recently in 2015 by 13-member interdisciplinary expert panel using modified Delphi method. The important changes in the new version are the lists of drugs to be avoided or dose adjustment based on the renal function and drug-drug interactions associated with harms in an elderly population.<sup>20</sup> Only one earlier Indian internal medicine studies explored the PIM use as per the updated version of the Beers criteria.<sup>19</sup> However, it did not compare its effectiveness as a screening tool with other criteria. Another recent criterion is an European Union list of potentially inappropriate medications [EU(7) PIM list]: a list of potentially inappropriate medications for older people consented by experts from seven European countries.<sup>10</sup> EU(7) PIM list suggests dose adjustments and special considerations when PIM to be use and alternative drugs for PIM.<sup>10</sup> It has not been explored in India. No such specific PIM tools are available considering the availability of drugs in India. So, this study was designed to assess the use of PIM in elderly patients in internal medicine wards and medical ICU in a tertiary care teaching hospital of India using such two recently introduced criteria- Updated Beers Criteria (2015) and EU(7) PIM list (2015).

## METHODS

This cross-sectional study was carried out after obtaining the permission from the Institutional Human Ethic Committee (IHEC). The inpatient records were retrospectively collected after the IHEC permission. The consent waiver was obtained from the IHEC.

### Study population

All elderly patients  $\geq 65$  years of age group admitted in the internal medicine wards and medical ICUs of GMERS General Hospital, Gotri between 1<sup>st</sup> July 2017 and 14<sup>th</sup> August, 2017.

### Selection criteria

All elderly inpatients admitted for  $>24$  hrs and received at least one prescribed medication were included in the study. Patients only admitted for observation were excluded from the analysis.

Data were collected in a case record form about patient's demographic details, diagnoses, hospital stay duration, treatment, related investigations and outcome. All prescribed drugs were labelled according to World Health Organization- anatomical therapeutic chemical (WHO-ATC) classification. The prescribed drugs were screened for the PIM (if present) using the updated Beer's Criteria (2015) and EU(7) PIM list (2015).<sup>10,20</sup>

### Outcome measures

Primary outcome variable was to estimate prevalence of PIM in the elderly patients as per updated Beer's Criteria

(2015), EU(7) PIM list (2015) and overall PIM prevalence. We used a total number of elderly patients receiving at least one PIM as numerator and total number of elderly patients as a denominator to estimate prevalence as per updated Beer's Criteria (2015) and EU(7) PIM list (2015). In case of the overall PIM prevalence, total number of elderly patients receiving at least one PIM identified by any one of the EU(7) PIM list and Beers criteria was considered as numerator.

Secondary outcome variables were to compare updated Beer's Criteria (2015) and EU(7) PIM list (2015) for the average number of PIM per patient, total number of PIM identified, WHO-ATC drug class system, underlying disorders in which PIM was used. Other secondary outcome variables screened as per Beer's criteria were WHO-ATC drug class pattern of PIM for the 'potential drug-disease or drug-syndrome interaction' that may exacerbate the disease or syndrome, drugs to be used with caution, clinically important 'drug-drug interactions' to be avoided, drug to be avoided or dosage to be reduced in the presence of renal dysfunction and use of drugs with strong anticholinergic property. As per EU(7) PIM list (2015), 'questionable PIM' were also screened. The 'questionable PIM' means those drugs on which no consensus among expert panellist of EU(7) PIM group was reached on the appropriateness of use in the elderly.

### Data analysis

All data were extracted into Microsoft excel sheet and cross-checked for the accuracy. We used percentage to present the data on prevalence of PIM, commonly used PIM, common diseases in which PIM was prescribed. We used mean (standard deviation-SD) to present the data of age, total number of drugs prescribed per patient and number of PIM prescribed per patient. We compared continuous data using unpaired t-test and categorical data using Chi-square test/Fisher's exact test. All statistical analysis was performed using GraphPad InStat demo version (San Diego, CA 92108, USA).  $P < 0.05$  was considered as statistically significant difference.

## RESULTS

### General characteristics of patients

Out of 1603 patients admitted in Internal medicine wards and ICU during study period, 258 patients were geriatrics. Thirty-three patients were excluded due to  $<24$  hr hospital stay. A total of 225 patients were included in this study. Male patients were 118 and female patients were 107 (M/F ratio=1.10). Twenty-one patients were admitted in ICUs. The mean age of the patients was 71.48 years (SD-6.42) with the age range of 65 to 92 years. The average number of drugs prescribed per patient was 11.95 (SD-4.28; range:4-12).

The most frequent diagnosis of study population admitted in wards were chronic obstructive pulmonary disease

(COPD)- 52 (25.49%), ischaemic heart disease (IHD)- 36 (17.64%), cerebrovascular stroke (CV stroke)- 27 (12%), dilated cardiomyopathy (DCM)- 18(8.82%), lower respiratory tract infection (LRTI)- 10 (4.90%), while ICU patients were admitted mainly for COPD- 7 (33.33%), IHD- 5 (23.80%) and pleural effusion- 4 (16.66%). The

commonly observed comorbidities were hypertension- 66 (29.33%) and diabetes mellitus (DM)- 51 (22.66%) (Table 1). The clinical diagnoses and co-morbidities were not significantly differ in patients receiving PIM as per EU(7) PIM list and Beers criteria.

**Table 1: Demography and clinical characteristics of study participants, and their comparison among patients receiving PIM as per EU(7) PIM list and Beers criteria.**

Variables	All patients n=225	Patients receiving PIM as per EU(7) PIM list n=112	Patients receiving PIM as per Beers criteria n=49	P values (Beers criteria vs. EU(7) PIM list)
Age, years Mean (SD)	71.48 (6.42)	72.10 (6.58)	71.12 (6.67)	0.38
Male gender n (%)	118 (52.44%)	54 (48.21%)	23 (46.93%)	0.88
Prescribed medications per patient Mean (SD)	11.95 (4.28)	13.29 (4.28)	14.26 (5.03)	0.21
PIM prescribed per patient Mean (SD)	0.81 (1.04)	0.71 (0.8)	0.28 (0.61)	0.001
PIM prevalence n (%)	118 (52.44)	112 (49.77%)	49 (21.77%)	<0.0001
Clinical diagnosis n (%)				
COPD	59 (26.22)	26 (23.12)	08 (16.32)	0.44
IHD	41 (18.22)	21 (18.75)	08 (16.32)	0.89
CV stroke	27 (12.00)	15 (13.39)	06 (12.24)	0.84
DCM	19 (8.44)	17 (15.18)	12 (24.49)	0.23
LRTI	11 (4.88)	06 (5.35)	02 (4.08)	1.00

p- value by unpaired t-test for continuous data and Chi-square test/Fisher's exact test for categorical data.

PIM - Potentially inappropriate medications; COPD- chronic obstructive pulmonary disease; IHD- ischaemic heart disease; CV - cerebrovascular; DCM - dilated cardiomyopathy; LRTI - lower respiratory tract infection.

### **PIM prevalence**

Overall use of at least one PIM was identified in 118 patients (52.44%). The prevalence of PIM in internal medicine wards and ICUs were 51.96, and 57.14 percent, respectively. EU(7) PIM list and Beers criteria suggested 86.94% and 34.23% of total PIM, respectively. EU(7) PIM list suggested significantly higher number of patients receiving at least one PIM as compared to Beers criteria [112 vs. 29,  $p < 0.0001$ ]. The prevalence of PIM using EU(7) PIM list and Beers criteria were 49.77 and 21.77 percent, respectively. The average number of PIM prescribed per patient was also significantly higher as per EU(7) PIM list than Beers criteria (0.71 vs. 0.28,  $p=0.001$ ) (Table 1).

### **Use pattern of PIM (Beers criteria versus EU(7) PIM list)**

A total of 184 PIM belonged to 33 different medications were used in study population. EU(7) PIM list suggested

160 (86.94%) PIM of 26 different medications. Beers criteria suggested 63 (34.23%) PIM of 15 different medications. Only a total of 39 (21.90%) PIM of 8 different medications were found present in both the list. In case of internal medicine wards, Beers criteria suggested 58 PIM of 15 different medications and EU(7) PIM list identified 145 PIM of 25 different medications use. While in case of ICU, use of 5 PIM of different 5 medications were suggested by Beers criteria and 16 PIM of 9 different medications as per EU(7) PIM list.

The PIM, present in both lists, belonged to NSAIDs (autacoids), anticholinergics (autonomic nervous system), cardiac glycosides (cardiovascular system), antihistaminics, central alpha blocker. Additionally PIM identified by EU(7) PIM list belongs to cough suppressant (respiratory system), drugs for peptic ulcer and GERD (gastrointestinal system), blood glucose lowering agent (endocrine system) and potassium sparing diuretic. Common disorders in which PIM use were observed were

COPD- 27(12%), IHD- 23(10.22%), DCM-17(7.55%), CV stroke- 12(5.33%), LRTI- 6(2.66%). The commonly involved systems were respiratory- 94(41.77%),

cardiovascular- 91(40.44%) and central nervous system- 37(16.44%).

**Table 2: Potentially inappropriate medications (PIM) identified by using the Beers criteria 2015 and the EU(7) PIM list 2015.**

Groups	Drugs	ATC code	Number of patient prescribed in wards (%)	Number of patient prescribed in ICU (%)
Gastrointestinal tract			29 (14.21)	08 (38.09)
Drugs for peptic ulcer and GERD*	Ranitidine <sup>2</sup>	A02BA02	24 (11.76)	01 (4.76)
	Famotidine <sup>2</sup>	A02BA03	-	01 (4.76)
Laxatives	Liquid paraffin <sup>2</sup>	A06AA01	02 (0.98)	03 (14.28)
	Sodium picosulfate <sup>2</sup>	A06AB08	01 (0.49)	02 (9.52)
Propulsives	Metoclopramide <sup>1,2*</sup>	A03FA01	02 (0.98)	01 (4.76)
Respiratory system			28 (13.72)	03 (14.28)
Cough and cold preparation	Dextromethorphan <sup>2</sup>	R05DA09	27 (13.23)	03 (14.28)
Adrenergics for systemic use	Terbutaline(oral) <sup>2</sup>	R03CC03	01 (0.49)	-
Cardiovascular system			25 (12.25)	04 (19.04)
Cardiac glycoside	Digoxin <sup>1,2</sup>	C01AA05	10 (4.90)	-
Central alpha blockers	Clonidine <sup>1,2</sup>	C02AC01	03 (1.47)	01 (4.76)
Antiarrhythmics	Amiodarone <sup>1,2</sup>	C01BD01	01 (0.49)	-
Other cardiac preparations	Ivabradine <sup>2</sup>	C01EB17	01 (0.49)	-
Diuretics	Spironolactone <sup>2</sup>	C03DA01	10 (4.90)	03 (14.28)
Endocrine system			27 (13.23)	-
Blood glucose lowering drugs	Glipizide <sup>2</sup>	A10BB07	23 (11.27)	-
	Glimepiride <sup>2</sup>	A10BB12	03 (1.47)	-
	Pioglitazone <sup>2</sup>	A10BG03	01 (0.49)	-
Central nervous system			22 (10.78)	01 (4.76)
Antiepileptics	Phenytoin <sup>2</sup>	N03AB02	05 (2.45)	01 (4.76)
Benzodiazepines (BZDs)	Lorazepam <sup>1*</sup>	N05BA06	03 (1.47)	-
	Alprazolam <sup>1*</sup>	N05BA12	02 (0.98)	-
Tricyclic antidepressants (TCAs)	Amitriptyline <sup>1*</sup>	N06AA09	02 (0.98)	-
Antipsychotics	Prochlorperazine <sup>2</sup>	N05AB04	02 (0.98)	-
	Haloperidol <sup>1,2</sup>	N05AD01	02 (0.98)	-
	Olanzapine <sup>1*</sup>	N05AH03	01 (0.49)	-
Psychostimulant, agent for ADHD, nootropics	Piracetam <sup>2</sup>	N06BX03	01 (0.49)	-
Centrally acting muscle relaxants	Tizanidine <sup>2</sup>	M03BX02	01 (0.49)	-
Opioids	Tramadol <sup>2</sup>	N02AX02	03 (1.47)	-
Anticholinergics			21 (10.29)	02 (9.52)
First generation antihistaminics	Chlorpheniramine <sup>1,2</sup>	R06AB04	07 (3.43)	-
	Promethazine <sup>1</sup>	R06AD02	01 (0.49)	-
Antispasmodic	Dicyclomine <sup>1</sup>	A03AA07	10 (4.90)	01 (4.76)
	Atropine <sup>1</sup>	A03BA01	01 (0.49)	01 (4.76)
	Hyoscine <sup>1,2</sup>	A03BA03	02 (0.98)	-
Non-steroidal anti-inflammatory drugs (NSAIDs)			12 (5.88)	01 (4.76)
	Diclofenac <sup>1,2</sup>	M01AB05	11 (5.39)	01 (4.76)
	Aceclofenac <sup>2</sup>	M01AB16	01 (0.49)	-
Antibacterial for systemic use			01 (0.49)	-
Quinolone antibacterials	Ofloxacin <sup>2</sup>	J01MA01	01 (0.49)	-

<sup>1</sup>as per Beers criteria; <sup>2</sup>as per EU(7)PIM list; ICU - intensive care unit; ATC - Anatomical therapeutic classification; ADHD- Attention deficit hyperactivity disorder; GERD- Gastroesophageal reflux disease; <sup>1\*</sup> Lorazepam, Alprazolam Amitriptyline Olanzapine and Metoclopramide were used in appropriate doses as per for elderly EU(7) PIM list, thus only included in Beers criteria

**Table 3: Questionable PIM as per EU(7) PIM list.**

Drugs	ATC Code	Total cases in wards (%)	Total cases in ICU (%)
Ipratropium bromide (inhaled)	R03BB01	72 (35.29)	09(42.85)
Amlodipine	C08CA01	57 (27.94)	03(14.28)
Aspirin low dose in primary prevention of cardiovascular disease	B01AC06	20 (9.80)	03(14.28)
Levofloxacin	J01MA12	16 (7.84)	01(4.76)
Ciprofloxacin	J01MA02	15 (6.66)	-
Metformin (>2x850mg)	A10BA02	03 (1.33)	-
Gabapentin	N03AX12	03 (1.33)	-
Pregabalin	N03AX16	03 (1.33)	-
Carvedilol	C07AG02	02 (0.88)	-
Tamsulosin	G04CA02	02 (0.88)	-

PIM- Potentially inappropriate medications; ATC - Anatomical therapeutic classification; ICU - intensive care unit

The commonly prescribed PIM were dextromethorphan (13.33%), ranitidine (11.11%), glipizide (10.22%), spironolactone (5.77%) and diclofenac (5.33%). All were included in EU(7) PIM list. Beers criteria suggested diclofenac only. The commonly prescribed PIM as per Beers criteria were diclofenac (5.33%), dicyclomine (4.88%), digoxin (4.44%), chlorpheniramine (3.11%) and clonidine (1.77%). All of them were present in EU(7) PIM list except dicyclomine. Lorazepam, alprazolam, amitriptyline, olanzapine and metoclopramide (2 patients) were considered inappropriate as per Beers criteria. They were not considered PIM as per EU(7) PIM list due to their appropriate dosage selection (Table 2).

**Table 4: PIM to be used with cautions in older adults as per Beers criteria.**

Groups	Drugs (ATC)	Rationale	Total cases in wards (%)	Total cases in ICU (%)
Diuretics	Furosemide(C03CA01)	Hyponatremia	24 (11.76)	08 (38.09)
	Spironolactone(C03DA01)		07 (3.43)	01 (4.76)
	Torasemide(C03CA04)		01 (0.49)	01 (4.76)
	Chlorthalidone(C03BA04)		01 (0.49)	-
Antipsychotics	Haloperidol(N05AD01)		01 (0.49)	-
	Olanzapine(N05AH03)		01 (0.49)	-
SSRIs	Fluoxetine(N06AB03)		01 (0.49)	-
TCAs	Amitriptyline(N06AA09)		01 (0.49)	-
Platelet aggregation inhibitor	Aspirin(B01AC06) for primary prevention of cardiac events in adults aged ≥80	Lack of evidence of benefit versus risk in adults aged ≥80	-	01 (4.76)

PIM - Potentially inappropriate medications; ATC - Anatomical therapeutic classification; ICU - intensive care unit; SSRI- Selective serotonin reuptake inhibitors; TCAs- Tricyclic antidepressants

### Use of 'questionable PIM' as per EU(7) PIM list

Total number of the 'questionable PIM' identified by EU(7) PIM list were 209 of different 10 medications. As shown in Table 3, commonly used medications of this category were ipratropium bromide(inhaled) (36%), amlodipine (26.66%), aspirin low dose in primary prevention of cardiovascular disease (10.22%), levofloxacin (7.55%) and ciprofloxacin (6.66%).

### Drug to be used with caution in elderly (Beers criteria)

As shown in Table 4, commonly identified drugs to be used with caution were furosemide (14.22%), spironolactone (3.55%), torasemide (0.88%). All three diuretics used in patients having hyponatremia.

### Drug-disease and drug-drug interaction (Beers criteria)

A total of 8 'drug-disease or drug-syndrome' interactions were identified that may exacerbate the disease or syndrome. Those were use of diltiazem in patients of heart failure; use of haloperidol and olanzapine (antipsychotics), lorazepam (benzodiazepines), hydrocortisone and budesonide (corticosteroids), and ranitidine (H<sub>2</sub> receptor antagonist) in patients of delirium; and use of chlorpheniramine (strong anticholinergic drug) in patient of benign prostatic hyperplasia. The potentially clinically important 'drug- drug interactions' that should be avoided in older adults were the concomitant use of drugs having anticholinergic (3.11%) actions (Table 5).

### Use of drugs according to renal functions (Beers criteria)

The most commonly used non-anti-infective medications that should be avoided or their dosage reduced as per kidney function in older adults was ranitidine- 38(16.88%) with CrCL of <50 mL/min. Other drugs were spironolactone- 1(0.44%) and enoxaparin-1(0.44%) with CrCL of <30 mL/min.

**Table 5: Clinically important non-anti-infective drug-drug interactions that should be avoided in older adults as per Beers criteria.**

Object drug class	Interaction drug class	Total cases in wards (%)	Total cases in ICU (%)
Anticholinergic	Anticholinergic	07 (3.43)	-
Dicyclomine	Chlorpheniramine, Hyoscine, Amitriptyline, Promethazine (1 each)	04 (1.96)	-
Ipratropium bromide(inhaled)	Chlorpheniramine, Dicyclomine, Olanzapine (1 each)	03 (1.47)	-
Benzodiazepines	≥2 other CNS active drugs	02 (0.98)	-
Lorazepam	Haloperidol+ Olanzapine, Haloperidol + Promethazine (1 each)	02 (0.98)	-
Others			
Tamsulosin	Furosemide	01 (0.49)	-
Hydrocortisone	Diclofenac	01 (0.49)	01 (0.49)

ICU - intensive care unit

**Drugs with strong anticholinergic properties (Beers criteria)**

Drugs with strong anticholinergic were dicyclomine-11(4.88%), chlorpheniramine- 6(2.66%), amitriptyline-3(1.33%), atropine(iv)- 2(0.88%), hyoscine(iv)- 2(0.88%), prochlorperazine-2(0.88%), promethazine-1(0.44%) and olanzapine-1(0.44%).

**DISCUSSION**

This study was designed to assess prevalence of PIM and to compare two PIM criteria in elderly patients admitted in a tertiary care teaching hospital in India. Our findings suggest PIM is an important area of concern for the drug use in elderly Indian inpatients. EU(7) PIM list helped to identify more number of PIM in this study population than Beers criteria.

The prevalence of PIM was significantly varied by two fold between Beers criteria (21.77%) and EU(7) PIM list (49.77%). This observed difference could be due to common use of drugs like dextromethorphan, ranitidine, glipizide and spironolactone in this set up. These drugs were considered PIM as per EU (7) list but not included in Beers criteria. The EU(7) PIM list includes most of the PIM present in Beers criteria. This suggests more sensitivity of EU(7) PIM list to detect PIM than Beers criteria. EU(7) PIM list also offers advantages in terms of dosage adjustment/titration, appropriate indications and use of alternative drugs. The Beers criteria tool offers an easy evaluation of drug-disease, drug-drug interactions and drugs to be used cautiously in the presence of altered renal functions.

Dextromethorphan is considered PIM due to its doubtful efficacy.<sup>10,11</sup> Ranitidine is considered PIM due to availability of better alternative (PPI) and evidence of uncommon but significant adverse effects like lethargy,

somnolence and disorientation with its use.<sup>10,21</sup> This is particularly problematic in older patients with impaired renal function with the dose of >150mg/24h(oral) or 50mg/24h(iv).<sup>10</sup> Its dose should be reduced in patients with altered renal function (<50CrCL/min.).<sup>20</sup> The preference of ranitidine over PPI seen in this setup could be due to economic reason. Ranitidine is available through Government supply in this set up. The literature suggests glipizide is comparable to metformin (1.82% decrease in HbA1c vs 2%) in type 2 DM patients.<sup>22,23</sup> In this study, glipizide was considered PIM due to inappropriate dose titration and the risk of protracted hypoglycaemia with its use.<sup>10</sup> EU(7) PIM list suggest metformin or gliclazide as an alternative to glipizide. Spironolactone have higher risk of hyperkalaemia and hyponatremia, especially if doses >25mg/d.<sup>10</sup> It requires monitoring of the serum Na<sup>+</sup> to adjust the dose and should be avoided in patients with CrCL<30mL/min.<sup>20</sup> Recent study suggest that higher dose of the spironolactone was well tolerated without any improvement in primary or the secondary outcomes.<sup>24</sup> Diclofenac is associated 2.5 folds higher risk of gastrointestinal bleeding than paracetamol and ibuprofen.<sup>25</sup> It shares equal risk of gastrointestinal bleeding with naproxen. To reduce gastrointestinal risk, it should be started with low dose (50 mg/d) with concomitant PPIs. The alternatives are paracetamol, ibuprofen (≤3x400mg/d or for a period shorter than 1week), naproxen (≤2x250mg/d or for a period shorter than 1week).<sup>10</sup> The other problem with diclofenac use in elderly is 1.2 to 2 folds higher risk of cardiovascular events than paracetamol and ibuprofen.<sup>10,25</sup> Dicyclomine was considered PIM due to its strong anticholinergic action and uncertain effectiveness as antispasmodic. It also interacts with the other anticholinergics that increases the risk of cognitive decline.<sup>20</sup>

In this study, commonly used 'questionable PIM' were ipratropium bromide, amlodipine and aspirin. Inhaled anticholinergics effectively control the COPD exacerbations and improves the quality of life.<sup>26,27</sup>

However, they increase the risk of cardiovascular morbidity and mortality.<sup>28,29</sup> They require cautious use in patients having cardiac disorders. Amlodipine is well tolerated and effective antihypertensive.<sup>30</sup> It can be prescribed in the comorbid conditions of hypertension.<sup>31</sup> However, literature suggests variable effect of amlodipine in patients of heart failure.<sup>32</sup> Recently one study suggest low dose aspirin do not effective as primary prevention of cardiovascular diseases and increases the risk of major haemorrhage.<sup>33</sup>

The most commonly used drug belonged to the category of 'drug to be used with caution' was diuretics. They increases the risk of hospitalizations due to risk of hyponatremia, hypokalaemia and decrease in the GFR.<sup>20,34</sup> Antipsychotics (typical and atypical) increases the risk of the hyponatremia and requires serum Na<sup>+</sup> level monitoring.<sup>35,36</sup> Antidepressants selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI), tricyclic antidepressants (TCA) are also associated with the hyponatremia, but more with SSRI compared to the TCA.<sup>37</sup>

In case of drug-disease interaction, diltiazem (non-dihydropyridine CCB) increases the risk of hospitalization in heart failure patients.<sup>38</sup> It may worsen constipation and increases the risk of bradycardia.<sup>10</sup> In a patient of delirium, antipsychotics increase the risk of confusion, hallucinations, delusions; prolongation of the QT interval and metabolic complications; benzodiazepines itself increases the risk of delirium, confusion, agitation and paradoxical excitation, respiratory depression.<sup>39-42</sup> Ranitidine and corticosteroids have low to moderate risk for the occurrence of delirium. Prescription of the strong anticholinergics may decrease the urinary flow and aggravate the symptoms.<sup>20</sup> Anticholinergics increases the risk of cognitive decline and the dementia in elderly patients.<sup>20,43</sup> Concurrent use of  $\geq 2$  CNS active drugs (more with SSRI and TCA) in elderly are associated with risk of falls and fractures.<sup>8,44</sup>

This study has several limitations. This study findings are based on use of medications in elderly patients admitted in one of the tertiary care teaching Government hospital of India. Due to retrospective study design, we could not assess drug rationality and inter-individual variations in drug selection. We could not identify use of PIM leading to adverse drug reactions due to absence of its documentations in case records.

## CONCLUSION

PIM are frequently used in the elderly. The commonly used PIM were dextromethorphan, ranitidine, glipizide, spironolactone and diclofenac. EU(7) PIM list identifies more number of PIM than Beers criteria in this study population. Clinician should use EU(7) PIM tool in their practice to avoid inappropriate drugs and to find their safer alternative drugs.

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