Utilization of potentially inappropriate medications in elderly patients in a tertiary care teaching hospital in India

**INTRODUCTION**

Inappropriate prescribing is a failure to provide quality medical care that should be achieved in standard clinical practice.[1] It includes over- and under-prescribing that may result in increased morbidity, hospitalization, and even death. However, the selection of appropriate medication in the elderly people may be a challenging and complex process, leading to increased risk of inappropriate prescribing.[2] Medication is considered as potentially inappropriate in the elderly when the risk of adverse drug event exceeds its expected clinical benefit even when better-tolerated alternatives are available.[3] Benzodiazepines, antihistamines, anticholinergics, and cardiac glycosides are the commonly prescribed inappropriate medicines among geriatric patients.[4,5]

Several drug- or disease-oriented validated tools have been developed to identify potentially inappropriate prescribing in the elderly. They may be applied with minimal clinical evaluation and many of them are from North America [e.g. Beer’s criteria, Improved Prescribing in the Elderly Tool (IPET)].[6,7] The Beer’s criteria were developed through an extensive literature review with a...
RESULTS

A total of 676 geriatric patients were admitted for treatment in the medicine ward during the study period, of whom 52.12% patients were females and 47.88% were males. The average age of geriatric patients was 72.69 years (95% CI: 72.12-73.27). A total 160 (23.76%) patients were more than 80 years of age. The common indications for the admission were ischemic heart disease (39.49%), hypertension (37.27%), cerebrovascular stroke (27.81%), diabetes mellitus (18.49%), and congestive heart failure (14.79%). The average number of total drugs prescribed per patient was 9.37 (95% CI: 9.09-9.64).

According to Beer’s criteria, at least one potentially inappropriate medication was prescribed in 590 (87.3%) patients. There were a total of 340 (56.6%) female patients. The average potential inappropriate medication prescribed per patient was 2.62 (95 CI: 2.50-2.74). As shown in Table 1, metoclopramide (54.29%), alprazolam (9.02%), diazepam (7.99%), digoxin >0.125 mg/day (5.03%), and diclofenac (3.7%) were the commonly used inappropriate medications. A total of 14 medications that can exacerbate the disease due to drug–disease interaction were observed in the records of 128 (18.9%) patients. Use of nonsteroidal anti-inflammatory drugs (NSAIDs) in heart and renal failure patients was the commonly identified drug-disease interaction [Table 2]. Totally eight drugs, which are to be used with caution in geriatric patients, were used. Isosorbide dinitrate (47.48%) and aspirin (14.05%) prescribed in patients more than 80 years of age were the commonly prescribed drugs requiring cautious use in elderly patients as per the Beer’s criteria [Table 3].

According to PRISCUS list, at least one inappropriate medication was prescribed in 210 (31.06%) cases. Totally 51% were female patients. A total of 26 and 9 medications were potentially inappropriate by Beer’s criteria and PRISCUS list, respectively. All nine drugs (chlorpheniramine, prazosin, clonidine, digoxin, nifedipine immediate release, amitriptyline, fluoxetine, alprazolam, and diazepam) identified by PRISCUS were a part of Beer’s criteria. PRISCUS list has identified inappropriate medications mainly from drugs acting on the central nervous system (CNS) and the cardiovascular system (CVS). Of the drugs acting on the CNS and CVS, it does not include antipsychotics (haloperidol and chlorpromazine), diuretics (spironolactone >25 mg/day), and amiodarone. Additional drugs screened by the Beer’s criteria were drugs with anticholinergic property (promethazine, benzhexol, dicyclomine), pain medications (NSAIDs, pentazocine, methocarbamol), metoclopramide, and mineral oil.
DISCUSSION

The present study evaluated geriatric in-patients for the pattern of potential inappropriate medications. In our setup, a total of 26 potentially inappropriate medications mentioned in the Beer’s criteria 2012 had been used. Use of at least one inappropriate medicine was quite higher (92.5% vs. 24%) in contrast to the reports of other studies from India. One possible reason could be the use of updated Beer’s criteria (2012) in the present study, wherein more number of potentially inappropriate medications have been classified than the previous list (2002). The commonly reported inappropriate medicine metoclopramide (54.3%) was not mentioned in the previous list of Beer’s criteria (2002). It is mainly used for gastroparesis and as an antiemetic because of its low cost. It was not used for chemotherapy-induced vomiting in our setup. Though it is approved for the treatment of gastroparesis, its use is largely considered inappropriate because of the possibility of extrapyramidal adverse reactions. Prolonged treatment with metoclopramide can cause serious adverse reactions like persistent tardive dyskinesia. Its incidence is as high as 15%. US Food and Drug Administration (FDA) has placed a black box warning because of the risk of tardive dyskinesia. Other risk factors for tardive dyskinesia, intended benefit, and duration of use should be considered while prescribing metoclopramide. However, it is not considered an inappropriate medicine by PRISCUS criteria. Other prescribed inappropriate medicines were benzodiazepines (20.4%), NSAIDs (8.6%), and digoxin (5%). Benzodiazepines, antihistamines, anticholinergic drugs, and cardiac glycosides were the potentially inappropriate medicines reported by Indian studies. Benzodiazepines are used for the treatment of insomnia and anxiety in the elderly. They can affect the cognitive functions. Their sedative effect is a risk factor for fall and fracture. Digoxin is mainly used for heart failure and atrial fibrillation. Altered pharmacokinetics enhances digoxin toxicity in the geriatric patients. Use of inappropriate medications is associated with increased risk of adverse drug reaction (ADR), morbidity, mortality, and economic burden to the patient.

Potentially inappropriate medication due to drug-disease or drug-syndrome interaction that may exacerbate the diseases should also be kept in mind. Prescription of NSAIDs in the heart and renal failure patients was the commonly identified potential drug-disease interaction. Use of NSAIDs should be restricted in the patients susceptible for congestive heart failure. It worsens the heart failure by salt and water retention and by increasing peripheral vascular resistance. It can deteriorate the renal function by affecting the prostaglandin synthesis.

Higher number of potentially inappropriate medicines was identified with Beer’s criteria than PRISCUS list (26 vs. 9). All nine drugs identified by PRISCUS list were included in the Beer’s criteria. This suggests the importance of Beer’s criteria for screening test to identify inappropriate medicines. However, many inappropriate medicines mentioned in the Beer’s criteria are not used in India (e.g. guanabenz, guanfacine, trimethobenzamide, brompheniramine, carboxyamine, guanidine, trimethobenzamide, and tiapride) as they are either not available in the Indian market or are not recommended by the Indian Council of Medical Research (ICMR) for use in geriatric patients.

Table 1: Potentially inappropriate medicines used in geriatric patients according to 2012 AGS Beer’s criteria and PRISCUS list

| Groups                        | Drugs                          | ATC code | Number (%) of patients prescribed |
|-------------------------------|--------------------------------|----------|-----------------------------------|
| Anticholinergic               | Chlorpheniramine               | R06AB04  | 1 (0.14)                          |
| First-generation antihistamines | Promethazine                  | R06AD02  | 14 (2.07)                         |
| Antiparkinsonism agents       | Trichexyphenidyl (benzhexol)   | N04AA01  | 3 (0.44)                          |
| Antispasmodic                 | Dicyclomine                    | A03AA07  | 12 (1.77)                         |
| Cardiovascular system         |                                |          |                                   |
| α2 Blocker                    | Prazosin                       | C02AC01  | 2 (0.29)                          |
| Central α agonist             |                                |          |                                   |
| Antiarrhythmic                | Amiodarone                     | C01BD01  | 14 (2.07)                         |
| Digitalis glycoside           | Digoxin>0.125 mg/day           | C01AA05  | 34 (5.03)                         |
| Dihydropyridines              | Nifedipine immediate release   | C08CA05  | 14 (2.07)                         |
| Potassium-sparing agent-diuretic | Spironolactone>25 mg/day       | C03DA01  | 3 (0.44)                          |
| Central nervous system        |                                |          |                                   |
| Tertiary TCA                  | Amlopiptyline                  | N06AA09  | 1 (0.14)                          |
| Antipsychotic                 | Haloperidol                    | N05AD01  | 14 (2.07)                         |
|                         | Chlorpromazine                 | N05AA01  | 4 (0.59)                          |
|                         | Alprazolam                     | N05BA12  | 61 (9.02)                         |
| Benzodiazepines short acting  | Lorazepam                      | N05BA06  | 20 (2.95)                         |
| Benzodiazepines long acting   | Clonazepam                     | N03AE01  | 3 (0.44)                          |
| Gastrointestinal tract system | Diazepam                       | N05BA01  | 54 (7.99)                         |
| Propulsive                    | Metoclopramide                 | A03FA01  | 367 (54.29)                       |
| Pain medication               |                                |          |                                   |
| Non-COX selective NSAIDs      | Aspirin+325mg/day              | B01AC06  | 22 (3.25)                         |
|                               | Diclofenac                     | M01AB05  | 25 (3.70)                         |
|                               | Ibuprofen                      | M01AE01  | 10 (1.48)                         |
| Opioid analgesic Skeletal muscle relaxants | Methocarbamol | M03BA03 | 1 (0.14) |

All drugs are included in Beer’s criteria, *Included in PRISCUS criteria, TCA = Tricyclic antidepressants, NSAIDs = Non-steroidal antiinflammatory drugs, AGS = American Geriatric Society, ATC = Anatomical therapeutic classification.

References:
[1] American Geriatric Society, ATC = Anatomical therapeutic classification.
[2] Other antihistamines, anticholinergic drugs, and cardiac glycosides were the potentially inappropriate medicines reported by Indian studies. Benzodiazepines are used for the treatment of insomnia and anxiety in the elderly. They can affect the cognitive functions. Their sedative effect is a risk factor for fall and fracture. Digoxin is mainly used for heart failure and atrial fibrillation. Altered pharmacokinetics enhances digoxin toxicity in the geriatric patients.
[3] Use of inappropriate medications is associated with increased risk of adverse drug reaction (ADR), morbidity, mortality, and economic burden to the patient.

Perspectives in Clinical Research | October-December 2014 | Vol 5 | Issue 4
meprobamate, etc.) and are reported in this study. The designation of certain drugs as inappropriate medicine is debatable. Use of amiodarone in the absence of other antiarrhythmic drugs and low-dose amitriptyline for neuropathic pain may be appropriate in a particular case.[21] No consensus was reached for amitriptyline as an inappropriate medicine in PRISCUS list. There is a need to create a separate list of potentially inappropriate medicines for India as for USA, Canada, France, Ireland, and Norway,[7,21-25] considering the prescribing pattern, approved drug list for Indian population, local availability, need for laboratory monitoring, and cost–benefit ratio of alternative drugs. Beer’s criteria also need to be compared with other tools to identify inappropriate medications, such as START (Screening Tool to Alert doctors to the Right Treatment) and STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) criteria, in an Indian setup.

Our data suggest that prescription of inappropriate medications is highly prevalent. Using tools for inappropriate medications should be routinely practiced to avoid potential inappropriate medications in geriatric patients. In one Italian study, use of inappropriate medications was significantly reduced by disseminating the list of drugs always to be avoided along with alternative drugs, reviewing the prescriptions, and through educating sessions.[26] Clinicians should always remember the possibility of adverse reactions while treating an elderly patient. Any new symptom should be considered drug related until proven otherwise.[27-29] The GerontoNet ADR risk score study reports that the risk of adverse reactions increases by fourfold with the number of medications ≥8. Other risk factors include history of adverse reactions, heart failure, liver disease, presence of four or more conditions, and renal failure.[30] In our study, approximately nine drugs were found to be prescribed per patient. For avoiding polypharmacy, the drug regimen should clearly be focused and prioritized on a particular goal to be achieved - prolonging longevity; reducing symptoms; minimizing medication burden, adverse effects, and costs.[31] “The Medication Appropriateness Index” is available to evaluate the inappropriate medications based on the following indications for the drug; effectiveness of drug for the condition; correct dosage and duration; correct and practical directions; possibility of clinically significant drug-drug interactions, drug-disease or drug-condition interactions; unnecessary duplication with other drugs; and being the least expensive alternative compared with others of equal usefulness.[31,32] Clinicians should be made aware of potential inappropriate medications used in geriatric patients by periodic evaluation. Prescribing guidelines can be made for the particular hospital for geriatric patients.

Table 2: Utilization potentially inappropriate medication used in geriatric patients due to drug-disease or drug-syndrome interaction that may exacerbate the disease or syndrome according 2012 AGS Beer’s criteria

| Disease                                           | Groups                           | Drugs               | ATC code  | Total cases(%) |
|---------------------------------------------------|----------------------------------|---------------------|-----------|---------------|
| Cardiovascular system                             |                                  |                     |           |               |
| Heart failure                                     | NSAIDs and COX2                  | Aspirin             | B01AC06   | 84 (12.43)    |
|                                                   | inhibitor                        | Diclofenac          | M01AB05   | 2 (0.29)      |
|                                                   | Non-dihydropyridine CCBs        | Verapamil           | C08DA01   | 3 (0.44)      |
| Central nervous system                            |                                  |                     |           |               |
| Delirium                                          | Anticholinergic                  | Dicyclomine         | A03AA07   | 1 (0.14)      |
|                                                   | Benzodiazepines                  | Alprazolam          | N05BA12   | 1 (0.14)      |
|                                                   | Corticosteroid                   | Hydrocortisone      | H02AB09   | 1 (0.14)      |
|                                                   | H2 receptor antagonist           | Famotidine          | A02BA03   | 1 (0.14)      |
|                                                   |                                   | Ranitidine          | A02BA02   | 4 (0.59)      |
| Dementia and cognitive disorder                   |                                  |                     |           |               |
| Kidney/urinary tract system                       | NSAIDs                           | Aspirin             | B01AC06   | 34 (5.03)     |
|                                                   | Anticholinergic                  | Dicyclomine         | A03AA07   | 1 (0.14)      |
|                                                   |                                   | Diclofenac          | M01AB05   | 1 (0.14)      |
| Lower urinary tract symptoms, BPH                 |                                  |                     |           |               |
|                                                   | Anticholinergic                  | Atropine            | A03AA01   | 3 (0.44)      |

NSAIDs=Non-steroidal anti-inflammatory drugs, CCBs=Calcium channel blockers, CRF=Chronic renal failure, ARF=Acute renal failure, BPH=Benign prostatic hyperplasia, AGS=American geriatric society

Table 3: Utilization of potentially inappropriate medication to be used with caution in geriatric patients according to 2012 AGS Beer’s criteria

| Group                | Drugs                      | ATC code  | Total cases(%) |
|----------------------|----------------------------|-----------|---------------|
| Vasodilators         | Nitroglycerine             | C01DA02   | 43 (6.36)     |
|                      | Isosorbide dinitrate       | C01DA08   | 321 (47.48)   |
|                      | Nifedipine (SR)            | C08CA05   | 16 (2.36)     |
|                      | Verapamil                  | C08DA01   | 6 (0.88)      |
|                      | Nicorandil                 | C01DX16   | 8 (1.18)      |
|                      | Prazosin                   | C02AC01   | 2 (0.29)      |
| Aspirin              | Aspirin in patients>80 years of age | B01AC06 | 95 (14.05)   |
| Antiepileptics       | Carbamazepine              | N03AF01   | 6 (0.88)      |
| SSRIs                | Fluoxetine                 | N06AB03   | 3 (0.59)      |

SR=Sustained released, SSRIs=Selective serotonin reuptake inhibitors, ATC=Anatomical therapeutic classification, AGS=American geriatric society
where separate geriatric clinics do not exist. Expert recommendations through computer-based feedback may help to reduce the number of medications.\[27]\n
There are several limitations of the study. Pattern of inappropriate medicine use only represents the usage in tertiary care teaching hospitals of India. Use of it can be different in primary, secondary, and specialized care institutions. Due to the retrospective nature of the study, rationality for the indications of potentially inappropriate medications could not be checked. There is a possibility of bias because of the lack of electronic prescription record system in our setup. There is no individualized evaluation of risk and benefit for each patient. Inappropriate medicines could have been prescribed because of poor tolerance of alternative drugs or possibility of drug interaction with them. Because of the lack of documentation of adverse events in indoor case papers, we could not estimate direct risk of adverse events due to potentially inappropriate medications in the elderly. The study has identified the potentially inappropriate medicines according to Beer’s criteria and PRISCUS list based on American and German populations, respectively. The possibility of adverse drug events may be differing in Indian population because of prescribing, environmental, and genetic differences.

CONCLUSION

It is an important screening tool to identify potentially inappropriate medications. The use of inappropriate medicines in the elderly patients is problematic. Clinicians should evaluate the medications they prescribe to geriatric patients using drug formularies.

ACKNOWLEDGMENT

Our sincere thanks go to Indian Council of Medical Research, New Delhi, India for selecting this study as a part of their short-term studentship 2012 program and providing scholarship to the student.

REFERENCES

1. Lund BC, Carnahan RM, Egge JA, Chrischilles EA, Kaboli PJ. Inappropriate prescribing predicts adverse drug events in older adults. Ann Pharmacother 2010;44:957-63.
2. Cahit C, Fahey T, Teeling M, Teljeur C, Feely J, Bennett K. Potentially inappropriate prescribing and cost outcomes for older people: A national population study. Br J Clin Pharmacol 2010;69:543-52.
3. Laroche ML, Charmes JP, Bouthier F, Merle L. Inappropriate medications in the elderly. Clin Pharmacol Ther 2009;85:94-7.
4. Harugeri A, Joseph J, Parthasarathi G, Ramesh M, Guido S. Potentially inappropriate medication use in elderly patients: A study of prevalence and predictors in two teaching hospitals. J Postgrad Med 2010;56:186-91.
5. Zaveri HG, Mansuri SM, Patel VJ. Use of potentially inappropriate medicines in elderly: A prospective study in medicine out-patient department of a tertiary care teaching hospital. Indian J Pharmaco 2010;42:95-8.
6. Page RL 2nd, Linnebur SA, Bryant LL, Ruscin JM. Inappropriate prescribing in the hospitalised elderly patient: Defining the problem, evaluation tools, and possible solutions. Clin Interv Aging 2010;5:75-87.
7. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Arch Intern Med 1997;157:1531-6.
8. 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;60:616-31.
9. Holt S, Schmiedl S, Thürrmann PA. Potentially inappropriate medications in the elderly: The PRISCUS list. Dtsch Arztebl Int 2010;107:543-51.
10. Sewell DD, Jeste DV. Metoclopramide-associated tardive dyskinesia. An analysis of 67 cases. Arch Fam Med 1992;1:271-8.
11. Lee A, Kuo B. Metoclopramide in the treatment of diabetic gastroparesis. Expert Rev Endocrinol Metab 2010;5:653-62.
12. Shaffer D, Butterfield M, Pamer C, Mackey AC. Tardive dyskinesia risks and metoclopramide use before and after U.S. market withdrawal of cisapride. J Am Pharm Assoc 2004;44:661-5.
13. Petrovic M, Marinam A, Warie H, Afschrift M, Pevernagie D. Is there a rationale for prescription of benzodiazepines in the elderly? Review of the literature. Acta Clin Belg 2003;58:27-36.
14. Mura T, Proust-Lima C, Akbaraly T, Amieva H, Tzourio C, Chevasssus H, et al. Chronic use of benzodiazepines and latent cognitive decline in the elderly: Results from the three-city study. Eur Neuropsychopharmacol 2013;23:212-23.
15. Dailly E, Bourin M. The use of benzodiazepines in the aged patient: Clinical and pharmacological considerations. Pak J Pharm Sci 2008;21:144-50.
16. Haas GJ, Young JB. Inappropriate use of digoxin in the elderly: How widespread is the problem and how can it be solved? Drug Saf 1999;20:223-30.
17. Hanratty CG, Mcclinchey P, Johnston GD, Passmore AP. Differential pharmacokinetics of digoxin in elderly patients. Drugs Aging 2000;17:353-62.
18. Hamilton HJ, Gallagher PF, O’Mahony D. Inappropriate prescribing and adverse drug events in older people. BMC Geriatr 2009;9:5.
19. McGettigan P, Han P, Jones L, Whitaker D, Henry D. Selective COX-2 inhibitors, NSAIDs and congestive heart failure: Differences between new and recurrent cases. Br J Clin Pharmacol 2008;65:927-34.
20. Page J, Henry D. Consumption of NSAIDs and the development of congestive heart failure in elderly patients: An underrecognized public health problem. Arch Intern Med 2000;160:777-84.
21. Gallagher P, Ryan C, Byrne S, Kennedy J, O’Mahony D, STOPP (Screening tool of older person’s prescriptions) and START (Screening tool to alert doctors to right treatment). Consensus validation. Int J Clin Pharmacol Ther 2008;46:72-83.
22. Pick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts. Arch Intern Med 2003;163:2716-24.
23. McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: A national consensus panel. CMAJ 1997;156:385-91.
24. Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: A French consensus panel list. Eur J Clin Pharmacol 2007;63:725-31.
25. Rognstad S, Brekke M, Feteavt A, Spigset O, Wyller TB, Straand J. The Norwegian general practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study. Scand J Prim Health Care 2009;27:153-9.
26. Keith SW, Maio V, Dudash K, Tempelin M, Del Canale S. A physician-focused intervention to reduce potentially inappropriate medication prescribing in older people: A 3-year, Italian, prospective,
proof-of-concept study. Drugs Aging 2013;30:119-27.

27. Steinman MA, Hanlon JT. Managing medications in clinically complex elders: “There’s got to be a happy medium”. JAMA 2010;304:1592-601.

28. Mallet L, Spinewine A, Huang A. The challenge of managing drug interactions in elderly people. Lancet 2007;370:185-91.

29. Rochon PA, Schmader KE, Sokol HN. Drug prescribing for older adults. 2013 Available from: http://www.uptodate.com/contents/drug-prescribing-for-older-adults. [Last accessed on 2013 Oct 20].

30. Onder G, Petrovic M, Tangisuran B, Meinardi MC, Markito-Notenboom WP, Somers A, et al. Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: The GerontoNet ADR risk score. Arch Intern Med 2010;170:1142-8.

31. Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. Arch Intern Med 2006;166:605-9.

32. Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, et al. A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992;45:1045-51.

How to cite this article: Jhaveri BN, Patel TK, Barvaliya MJ, Tripathi C. Utilization of potentially inappropriate medications in elderly patients in a tertiary care teaching hospital in India. Perspect Clin Res 2014;5:184-9.

Source of Support: Nil. Conflict of Interest: None declared.

Author Help: Online submission of the manuscripts

Articles can be submitted online from http://www.journalonweb.com. For online submission, the articles should be prepared in two files (first page file and article file). Images should be submitted separately.

1) First Page File:
Prepare the title page, covering letter, acknowledgement etc. using a word processor program. All information related to your identity should be included here. Use text/rtf/doc/pdf files. Do not zip the files.

2) Article File:
The main text of the article, beginning with the Abstract to References (including tables) should be in this file. Do not include any information (such as acknowledgement, your names in page headers etc.) in this file. Use text/rtf/doc/pdf files. Do not zip the files. Limit the file size to 1 MB. Do not incorporate images in the file. If file size is large, graphs can be submitted separately as images, without their being incorporated in the article file. This will reduce the size of the file.

3) Images:
Submit good quality color images. Each image should be less than 4096 kb (4 MB) in size. The size of the image can be reduced by decreasing the actual height and width of the images (keep up to about 6 inches and up to about 1800 x 1200 pixels). JPEG is the most suitable file format. The image quality should be good enough to judge the scientific value of the image. For the purpose of printing, always retain a good quality, high resolution image. This high resolution image should be sent to the editorial office at the time of sending a revised article.

4) Legends:
Legends for the figures/images should be included at the end of the article file.