

Prescribing in Elderly: A Science and an Art

Mahadev Desai*, Urman Dhruv*

Introduction :

The safe and effective use of medications in elderly population is a cornerstone of high-quality medical care. Longevity across the globe has improved markedly in last couple of decades reflecting improving standards of living, awareness about diseases, better diagnostic techniques and development of safer and better medicines. Improved survival means increased number of people becoming “older”. By definition “old” is person of age 60 years or more, while “Oldest old” is person of age 80 years or more. In 1990, the world’s population of people over 60 years old was 9.2%, which rose to 11.3% in 2013. It is estimated that by 2050, this figure would be about 21.2%.⁽¹⁾

With increasing longevity in years, there is corresponding increase in the burden of comorbidity and also increase in the consumption of medications. Appropriate selection and prescription of curative and preventative medicines is an essential element of high quality healthcare for older people.⁽²⁾ The proportion of drug consumption and health care resource consumption by geriatric population is much more than the proportion of the other population. Similarly, number of hospitalizations in geriatric population is outnumbering the young counterparts by huge margins. It is estimated that older people consume approximately 40% of all over-the-counter (OTC) medications sold in the United States.⁽³⁾ In addition, there is emerging evidence that the consumption of complementary and alternative medicines amongst older adults is steadily increasing.⁽⁴⁾

In this article, we discuss the challenges and complexities of prescribing for older people including, physiological differences in geriatric population, comprehensive geriatric assessment, prescribing criteria and clinically-relevant pharmacological interventions. However, this is not an exhaustive article and will include only important points.

1. Geriatric Population is different

Elderly patients are different in many ways from their younger counterparts, and most vulnerable group for development of adverse events with medicines.

- Altered Physiology
- Altered Immunity
- Presence of Multiple Comorbidities.
- Poly-therapy including use of Alternative “pathies” and herbal remedies
- Minimum or No Insurance coverage
- Limited scientific evidence for use of drugs in Elderly population. Most information is extrapolated from studies in younger population, as Elderly and very elderly are not included in most studies
- Common presentation with confusion, fall, depression or incontinence, known collectively as Geriatric Giants, for illness of any system making diagnostic approach much difficult.

2. Effect of aging on Pharmacokinetics of a drug

Prescribers must be aware of important age related anatomical, biochemical and physiological changes that affect Pharmacokinetics (Pk) and Pharmacodynamics (Pd) of drugs

Altered Pharmacokinetics (Pk) includes ADME (Absorption, Distribution, Metabolism and Elimination) while Pharmacodynamics (Pd) includes RPC (Receptor binding, Post receptor effects and Chemical reactions) of prescribed drugs (see Table 1)

Commonly prescribed drugs such as verapamil, amitriptyline and morphine may have higher bioavailability at standard doses in older people, thus leading to greater potential for adverse effects if not dose adjusted. An example of this includes the risk of first dose hypotension with antihypertensive medications that have a high extraction ratio. This ratio would be reduced in older patients thus leading to

* Consulting Physician, Ahmedabad

Correspondence : Dr. Mahadev Desai

E-mail : mahadevdesai@yahoo.com

Table 1: Common age related changes affecting pharmacokinetics of a drug in geriatric population. ⁽⁴⁾

Absorption:	↓ amount of saliva, ↑ gastric pH, ↓ gastric acid secretion, ↑ gastric emptying time, ↓ gastric surface area, ↓ gastrointestinal motility, ↓ active transport mechanisms.
Distribution	↓ cardiac output, ↑ peripheral vascular resistance, ↓ renal blood flow, ↓ hepatic blood flow, ↓ body water, ↑ body fat tissue, ↓ serum albumin, ↑ distribution of lipid soluble and ↓ distribution of water soluble drugs.
Metabolism:	↓ microsomal hepatic oxidation, ↓ clearance, ↑ steady state levels, ↑ half lives, and ↑ levels of active metabolites.
Excretion:	↓ in renal perfusion, ↓ in renal size, ↓ in glomerular filtration rate, ↓ tubular secretion and ↓ in tubular reabsorption.

Table 2: Effects of Age on Creatinine clearance in a male of 55.0 kg weight calculated by Cockcroft-Gault formula

Age in years	Serum Creatinine in mg%	eGFR in ml/min
30	1.2	70
50	1.2	57
70	1.2	45
90	1.2	32

greater bioavailability after hepatic extraction and thus greater potential for significant first-dose hypotension, so caution is needed when initiating antihypertensive treatment in an older patient with respect to dose and time of administration.

3. Effect of aging on Glomerular Filtration rate (GFR)

GFR should be estimated using readily available formulas such as the Cockcroft and Gault (CG) and Modification of Diet in Renal Disease (MDRD).⁽⁵⁾ Prescribers should be aware that serum creatinine concentration alone is an unreliable marker of renal function in the elderly owing to reductions in muscle volume as the age advances.⁽⁶⁾ (see Table 2).

4. Potentially Inappropriate Medication Use in Older Adults (Beers criteria or List)

Inappropriate prescribing (IP) is a commonly used term. It pertains to the inappropriate use of medications that may cause more harm than good; and also includes the under prescribing of clinically indicated medications.

Beers Criteria is the list of drugs which are periodically updated which include number of drugs which when prescribed in geriatric population may result in to more

harm than good and are better avoided in this population. The Beers Criteria are intended to improve medication selection, reduce adverse drug events, and provide a tool to assess cost, patterns, and quality of care of drugs used for people aged 65 years or older.

The American Geriatrics Society (AGS) has released the 2019 ⁽⁷⁾ update to the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. (Table 3)

Prolonged use of non-steroidal anti-inflammatory drugs should be avoided if possible among older adults,

5. Polypharmacy

Polypharmacy is often defined by the number of prescribed medications, with ≥ 6 drugs being a common cut off point.⁽⁸⁾ While poly-pharmacy most commonly refers to prescribed medications, it is important to also consider the number of OTC and herbal/supplements used. Prescription of multiple drugs impacts negatively on adherence and compliance. Clinicians are sometimes unaware of their patients' complete prescription record perhaps because of multiple prescribers or underreporting by patients at time of consultation.

Table 3: Few important notable features of Beers Criteria 2019 ⁽⁷⁾

Molecule	Action	Reason
H2 receptor antagonists	Should be avoided in older adults with or at high risk of delirium	Induces or worsening delirium
Dextromethorphan/quinidine	Used with caution	Increases risks of falls
Rivaroxaban	Cautious in patients above the age of 75 years	Increases risk of bleeding
Trimethoprim and sulfamethoxazole	Cautious when used with ACE -I or ARB in patients with CKD	Induces hyperkalemia
Carbamazepine, mirtazapine, oxcarbazepine, serotonin, norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, tramadol	Cautious in older patients	Can cause syndrome of inappropriate antidiuretic hormone secretion. Sodium measurement is a must
Serotonin and norepinephrine reuptake inhibitors	Caution for patients at risk of fall	
All antipsychotics has been revised to except quetia pine, clozapine, and pimavanserin.	Avoid in Parkinsonism	
Macrolides (except azithromycin) or ciprofloxacin	Not with Warfarin	Increased risk of bleeding
Ciprofloxacin	Impaired kidney function	Increased risk for tendon rupture and increased central nervous system effects.

Table 4: Risk of adverse drug reaction related to number of medicines consumed

Number of medicines	Risk of adverse drug reaction
2	13%
4	38%
7	82%

Table 5 : Important drug-drug interaction in geriatric population

Drugs		Interaction	Effect
Antihypertensive drugs	NSAIDs	NSAID antagonizes hypotensive effect	Reduced effect of antihypertensive medicines
Aspirin	Steroids or NSAIDs	Increased acid secretion	Peptic ulcer and bleeding
Digoxin	Diuretics	Hypokalemia	Digoxin toxicity and arrhythmias
Tricyclic anti depressants (TCA)	Enzyme inducers	Reduced clearance of TCA	Arrhythmias, confusion, orthostatic hypotension, falls

Table 6 : An example of Prescribing Cascade

Initial drug	Adverse reaction to drug	New drug initiated
Ramipril	Cough	Codeine
Codeine	Constipation	Laxative
Laxative	Electrolyte imbalance	Anti -psychotic drugs
Anti-psychotic drugs	Involuntary movements	Anti -parkinsons drugs

For a hypothetical older female patient with chronic obstructive pulmonary disease, type 2 diabetes, osteoporosis, hypertension, and osteoarthritis, clinical practice guidelines would recommend prescribing 12 medications for this individual.⁽⁹⁾

Poly-pharmacy has also been associated with decreased physical and cognitive capability, even after adjusting for disease burden. As the number of medicines goes on increasing, chances of adverse drug reaction increase and so are the chances of hospitalization. (Table 4)

6. Drug-Drug and Drug-Disease Interactions

One drug can interact with another drug through pharmacokinetic or pharmacodynamics mechanisms. (Table 5) A study of over sixteen hundred older outpatients across six European countries found that 46% had at an important drug interaction with 1 in 10 having the potential for severe consequence.⁽¹⁰⁾

Drugs from the groups like Antihistaminics, Anticholinergics, Antiarrhythmics (Amiodarone, Sotalol, Quinidine), tricyclic anti-depressants, Fluoroquinolones and Erythromycin can cause life threatening Q-T prolongation, especially when used

with Ondansetron in doses more than 32 mg per day.

Drugs can occasionally deteriorate existing disease. The risk of drug disease interactions is higher in older adults who are on multiple medications to treat multiple conditions

a) Analgesics

Paracetamol is safe up to 2 grams per day. One needs to check renal and liver function before increasing doses. Small dose of Tramadol is safe but one must remember dangerous interactions with Linezolid and SSRI.

b) Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs themselves increase blood pressure but reduce the effect of certain antihypertensive drugs like ACE-I or ARB. These drugs definitely increase the risk of hospitalization for heart failure. When eGFR is less than <30 mL/minute, it is better to avoid use of these drugs. When indicated, one should use the lowest dose for the shortest period. Diclofenac has shortest half-life while Naproxen and Piroxicam have longer half-lives.

c) Proton Pump Inhibitors (PPI) and H2 Receptor Blocker

Prolonged use of PPIs can cause Vitamin B12 deficiency, Magnesium deficiency, Osteoporosis & Fracture risk, ↑ rate of infections (C. difficile etc.), ↑ rate of AIN (Acute Interstitial Nephritis). When prescribed, ask patient to take PPIs, 30 to 60 minutes prior to breakfast (and dinner if twice-daily therapy is required) to maximize effectiveness.

d) Laxatives

Before initiating treatment with laxatives, always ensure to rule out secondary causes of constipation and drug induced constipation. Fecal impaction must be thought of and dealt with if diagnosed. Non pharmacological methods to avoid constipation must be practiced such as liberal use of fluids, fiber rich diet and then if required, first use Isapgul.

e) Antibiotics

Quinolones are not a drug of first choice for respiratory disease or for urinary tract disease. They are not as safe as they were once thought to be. They can cause CNS stimulation and can precipitate seizures in a predisposed patient. Q-T prolongation on ECG is common and may be life threatening. They can also cause hypoglycemia.

Aminoglycosides are nephrotoxic and ototoxic and should not be used as first line of treatment in diarrhea or in situations where fluid loss is suspected. When indicated, it is safer to give full dose as a single dose to reduce nephrotoxicity. In geriatric population, it is wiser to keep an eye on eGFR during treatment with aminoglycosides.

Linezolid and Azithromycin are infamous for their drug-drug interactions especially with Tramadol.

Doxycyclin, Azithromycin, Clindamycin, Rifampicin are known to stick to throat and requires to be taken with plenty of fluids in elderly patients.

f) Medicines for Bronchial asthma

Theophylline preparations are potentially very toxic in older people and must be used with caution especially when co-prescribed with Ciprofloxacin.

Beta agonist inhalers can cause dangerous hypokalemia especially when the patient is also receiving steroids and diuretics.

g) Medicines for hypertension

Beta blockers are less effective for hypertension in this age group. Short acting nifedipine is best avoided. ARB must be withheld at the first sign of fluid loss or preoperatively. Alpha blockers when used for hypertension can cause first dose phenomenon. Postural hypotension must be looked for in every visit. Stop Tamsulosin, especially before cataract surgery due to fear of intra-operative floppy iris syndrome (IFIS).

h) Medicines for diabetes

Short acting drugs are preferred. Doses of diabetes medicines need to be adjusted as per eGFR, applicable for most of gliptins and metformin. SGLT 2 Inhibitors and metformin should be withheld at the first signs of infection or fluid loss or prior to surgical procedures. Use of quinolones can cause unexpected hypoglycemia.

i) Cardiac medicines

Digoxin is the biggest culprit in this age group and must be used with caution, strictly with regular measurement of potassium and with ECG monitoring and if need be serum digoxin levels. Nitrites when given sublingually may cause hypotension and should be carefully watched for. Dual antiplatelet agents, when indicated, must be used under supervision and regular hemoglobin measurement and occasional stool examination for occult blood. Statins are safe in moderate doses.

j) Anticoagulant drugs

Warfarin is the most useful and yet the most dangerous drug for elderly population. It has the potentials for life threatening drug-drug interactions. Newer Oral Anticoagulants (NOAC) (Dabigatran, Rivaroxaban, Apixaban) are expensive but very safe and easy to titrate and manage. Compared to warfarin, NOACs are as, or more effective at reducing the risk of stroke & intracranial haemorrhage in patients with atrial fibrillation, but still increase risk of bleeding in older

adults particularly those with impaired renal function.

k) Sedatives and hypnotics

All drugs from this group have side effects of Cognitive impairment, increase in incidence of falls & fractures. Tolerance and Dependence develop on prolonged use. Non-benzodiazepine members have rapid & shorter duration of action. They do not disturb normal sleep pattern. They have less habit potential and lesser side effects with fewer rebound effects.

Avoid using antihistamines as sedatives or hypnotics as they have many undesirable anticholinergic effects, especially in elderly population.

l) Antipsychotics

Most antipsychotic drugs have significant side effects such as sedation, orthostatic hypotension, anticholinergic effects and akathisia (subjective motor restlessness). Drug-induced parkinsonism is well known and can persist for up to 6 to 9 months even after the drug is stopped. Extrapyrimalidal dysfunction can develop even with second generation antipsychotics like olanzapine, risperidone more so at higher doses.

m) Antidepressants

Efficacy of tricyclic antidepressants is same as newer generation drugs like SSRI and SNRIs but the latter group of medicines are safer. Paroxetine is more sedating than other SSRIs and has more anticholinergic effects. Doses of Escitalopram in geriatric population should be limited to a maximum of 10 mg/day, because of concern for QT prolongation. Venlafaxine may increase blood pressure. Mirtazapine may be sedating and may stimulate appetite and cause weight gain.

7. Prescribing cascade

A prescribing cascade develops when an ADE caused by a prescribed drug is misinterpreted as a new medical condition and additional drug is then prescribed to treat this medical condition. The patient is then at risk for developing additional ADEs related to the new and potentially unnecessary treatment. (Table 6)

8. Underprescribing

Underprescribing of essential medication is perhaps an even bigger concern than misuse of medications in older patients, particularly when the potential outcome of not treating the condition can be catastrophic e.g. failure to give evidence based anticoagulation in a case of atrial fibrillation with cardio embolic stroke, not correcting iron deficiency anemia in a patient with heart failure or not prescribing statins when indicated.

9. Tips for appropriate prescribing

1. First make a list of all the drugs prescribed by all the treating doctors. Obtain a complete drug history which should also include OTC medicines, dietary supplements and alternative medicines.
2. Consider non-pharmacological alternatives e.g. changes in diet, stop tobacco, alcohol.
3. Use the simplest dosing regimen (e.g., once a day prescription of a sustained preparation preferable to 2 to 3 times per day of the same drug). Start low, go slow. Use least expensive alternative.
4. Ensure each medication has an appropriate indication and a clear therapeutic goal (this involves careful clinical assessment and appreciation of time to obtain treatment effect and life expectancy of the patient).
5. Adjust doses for renal and hepatic impairment.
6. Avoid therapeutic duplication which happens when two doctors prescribe without seeing each other's prescription.
7. Provide verbal and written instructions on indication, time and route of administration and potential adverse effects of each medication.
8. Consider drug-drug and drug-disease interactions.
9. Reach therapeutic dose before switching / adding another drug.
10. Try not to start two drugs at the same time.
11. Consider drug as one of the causes in differential diagnosis (D/D) for any new symptom or sign that occurs after a drug is prescribed.
12. Never be the First or Last to prescribe a New Drug.
13. Beware and Be aware of Prescribing Cascade.

14. Include the patient (and care taker where appropriate) in prescribing decisions.
15. Never forget immunization in elderly population.

Conclusion:

Prescribing in elderly is a tricky situation, where the prescriber has to take in to consideration of multiple factors which are different than their younger counterparts. In elderly there is altered physiology; altered Pk and Pd of most drugs, altered immunity and reduced GFR. All have profound effects on the ultimate outcome of a prescription. The possibility of an adverse drug event (ADE) should always be at the back of mind when evaluating an older adult; any new symptom should be considered drug-related until proven otherwise.

Always keep in mind all the medicines that the patient is taking and this includes even the herbal preparations, dietary supplements and OTC medicines.

“Beers criteria” is a useful list for guidance while prescribing in elderly to judge the benefits versus the risk of prescribing drugs. However, one must be remember that they are not laws but just guiding principles and a physician should evaluate each case individually. Miss-utilization or over-utilization of medicines has to be condemned, but under-utilization of number of drugs like statins also must not be overlooked. Under-utilization of drugs, also frequently results from ignorance of treating doctor, misconcepts in patients’ minds and financial constraints.

A regular review of all the drugs prescribed to a patient on every visit is essential part of proper prescribing.

References:

1. United Nations. World Population Ageing 2013. Available from: URL: http://www.un.org/en/development/desa/population/publications/pdf/ageing/World_Population_Ageing_2013.pdf.
2. Chrischilles EA, Foley DJ, Wallace RB, Lemke JH, Semla TP, Hanlon JT, Glynn RJ, Ostfeld AM, Guralnik JM. Use of medications by persons 65 and over: data from the established populations for epidemiologic studies of the elderly. *J Gerontol* 1992; 47: M137-M144 [PMID: 1512428 DOI: 10.1093/geronj/47.5.M137].
3. Hanlon JT, Fillenbaum GG, Ruby CM, Gray S, Bohannon A. Epidemiology of over-the-counter drug use in community dwelling elderly: United States perspective. *Drugs Aging* 2001; 18: 123-131 [PMID: 11346126 DOI: 10.2165/00002512-200118020-00005].
4. Cheung CK, Wyman JF, Halcon LL. Use of complementary and alternative therapies in community-dwelling older adults. *J Altern Complement Med* 2007; 13: 997-1006 [PMID: 18047447 DOI: 10.1089/acm.2007.0527].
5. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; 130: 461-470 [PMID: 10075613 DOI: 10.7326/0003-4819-130-6-199903160-00002].
6. Corsonello A, Pedone C, Corica F, Mussi C, Carbonin P, AntonelliIncalzi R. Concealed renal insufficiency and adverse drug reactions in elderly hospitalized patients. *Arch Intern Med* 2005; 165: 790-795 [PMID: 15824299 DOI: 10.1001/archinte.165.7.790].
7. 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. Published online January 29, 2019. <https://onlinelibrary.wiley.com/doi/epdf/10.1111/jgs.15767>. Accessed February 1, 2019.
8. Bushardt RL, Massey EB, Simpson TW, Ariail JC, Simpson KN. Polypharmacy: misleading, but manageable. *ClinInterv Aging* 2008; 3: 383-389 [PMID: 18686760 DOI: 10.2147/CIA.S2468].
9. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. AU Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW SO *JAMA*. 2005;294(6):716.
10. Beard K. Adverse reactions as a cause of hospital admission in the aged. *Drugs Aging* 1992; 2: 356-367 [PMID: 1504448 DOI: 10.2165/00002512-199202040-00008].