Prescribing Challenges In The Elderly Patient

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Chairman: Dr. Chan TY
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Background

- Elderly people are at a high risk of experiencing problems with drug therapy due to:
  - 1) Age-related changes in the body (i.e., change in pharmacokinetic & pharmacodynamic)
  - 2) Exposure to many medications due to multiple health problems
  - 3) Social circumstances such as living alone, difficulty in visiting their primary physician
4) Failure to comply with the complicated drug treatment plan and poor understanding of the drug treatment

5) Confusion resulting from the use of multiple medications, memory problems and failing vision leading to impaired functioning
• Elderly patients take about three times as many medications as younger patients do.

• They are also the greatest consumers of prescribed & non-prescribed medications.

• Prescription medications can improve the symptoms of a disorder and improve the quality of life.

• However, they also have the potential to cause dangerous side effects, especially in elders.
4 Stories

• Polypharmacy
• Overdose of medicine / wrong drug administration
• Drug-drug interaction
• Drug adverse side effects
Case 1

- F/ 75, ex-smoker
- Lives with daughter, care by maid
- ADL independent
- Referred from other cluster for further FU
- PHx: COPD, gastritis, IHD, Hypertension, chronic back pain with vertebral collapse
- Recent RFT - Cr 100
- Echo showed satisfactory LV function
List of Medications

• Aspirin 160mg daily
• Lansoprazole 30mg daily
• MTCO 10ml tds
• Isordil 10mg tds
• Captopril 6.25mg tds
• Norvsac 7.5mg daily
• Frusemide 20mg daily
• Slow K 600mg daily
• MV 1 tab bd
Problems with this drug list?

- Costs a lot of money (although most drugs are not too expensive)
- Polypharmacy / Polymedicine
- Adverse drug reactions
- Prescribing cascade
Polypharmacy / Polymedicine in Elderly

• Definition of ‘polypharmacy’ varies - no consensus

• The most commonly cited definition was ‘medication did not match the diagnosis’

• Some definitions for polypharmacy place a value on the number of concurrent medications

• The most common referred number is 5 medication >= 5 drugs

Polypharmacy in HK elders

- Cross-sectional, retrospective study from Jan 2007 - Dec 2007
- 400 elderly patients
- ≥5 drugs defined as polypharmacy
- 65% of them had problem of polypharmacy
- Propoxyphene (7%), methyldopa (6%), anti-histamine (6%), calcium channel blockers with constipation (4%) & pseudoephedrine with HT (1%)

Prescribing Cascade > Polypharmacy

ACEI inhibitor

Postural hypotension, diagnosed as dizziness

Exacerbation of postural hypotension, leading to fall and subsequent fracture

Stemetil started
Other Common Prescribing Cascade

- Adalat retard or norvsac - lasix
- Diuretic - allopurinol
- NSAIDs - anti-hypertensives (66%)  
- Maxolon mimic Parkinson’s disease - carbidopa/ levodopa (3x)  
- Cholinesterase inhibitor for Alzheimer disease - oxybutynin (over 50%)  
• Vasodilators, diuretics, beta blockers, calcium channel blockers, ACE inhibitors, NSAIDs, opioid analgesics, sedatives, statins → Dizziness → Prochlorperazine

• Thiazide diuretics → Hyperuricaemia, gout → Allopurinol or colchicine

• Paroxetine, haloperidol → Tremor → Levodopa-carbidopa

• Erythromycin → Arrhythmia → Antiarrhythmics

• Antiepileptic → Rash → Topical corticosteroids

• Antiepileptic → Nausea → Metoclopramide, domperidone

• Digoxin, nitrates, loop diuretics, ACE inhibitors, oral corticosteroids, antibiotics, NSAIDs, opioid analgesics, methylxanthines (e.g. theophylline) → Nausea → Metoclopramide

• Antipsychotics → Extrapyramidal adverse effects → Levodopa, anticholinergic
Adverse Drug Reaction

• Patients are at the highest risk of having an adverse drug reaction **soon after** starting a medicine.

• About **90%** of patients who experience an adverse drug reaction report it within **four months** of starting a new drug, with **75%** of these patients having the adverse drug reaction within **1 month**.
• Many adverse drug reactions are dose related & starting therapy at high doses is associated with an increased risk of adverse reactions in the elderly

• Adverse drug reactions may also occur following dose increases

• About 15% of patients will stop treatment without advising their doctors

• ‘Start slow and go slow’ with medications
• When Rx reactions occur, non-drug treatment strategies are likely to be the most appropriate 1st line Mx, rather than starting 2nd Rx to counteract S/E

• Reducing the dose of Rx causing the adverse drug reaction is appropriate if the reaction is dose related

• Trying a different drug with a similar effect, but less risk of causing the adverse drug reaction, may be another way to avoid the prescribing cascade
Adverse Drug Reactions

- **Type A** reactions: dose related, account for most ADRs
- **Type B**: Idiosyncratic
- **Type C**: dose related, cumulative dose (HPA axis suppression by steroid)
- **Type D**: time related, deflated (tardive dyskinesia)
- **Type E**: withdrawal, end-of-dose
- **Type F**: unexpected failure of therapy
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• Lansoprazole 30mg daily
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• MV 1 tab bd

Overlapping

Should consider alternatives with less frequent dose

Prescribing cascade
Tools to Reduce Polypharmacy

- Beers criteria
- Improved Prescribing in the Elderly Tool (iPET)
- Medication appropriateness index (MAI)
- ARMOR tool
- **Good Palliative-Geriatric Practice algorithm**
- Patient-focused drug surveillance
- Geriatric Risk Assessment Medguide
- Prescribing Optimization Method
- Anticholinergic risk scale
More Tools

• Screening Tool to Alert Doctors to Right Treatments (START)

• Screening Tool of Older Persons’ Potentially Inappropriate Prescriptions (STOPP)
Beers Criteria

- Widely adopted in the US
- Created by expert consensus in 1991 originally intended to identify inappropriate medication in nursing home residents
- Pros: 1) incorporated with the most current evidence 2) easy to use & 3) can be used in both clinical and research setting
- Cons: 1) many of Rx are old & out of use 2) insufficient evidence to include some Rx on the list & 3) based on expert consensus, reliability is not ensured
<table>
<thead>
<tr>
<th>Drug</th>
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<th>Recommendation</th>
<th>Quality of Evidence</th>
<th>Strength</th>
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**Beers Criteria**

- **Drug**: Antipsychotics
- **Rationale**: May cause symptomatic hyperprolactinemia, extrapyramidal reaction, dystonia, tardive dyskinesia, akathisia, mydriasis, lethargy, parkinsonism, sedation
- **Recommendation**: Use with caution
- **Quality of Evidence**: Moderate
- **Strength**: Weak

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**Additional Notes**

- Greater risk of bleeding than will occur in adults aged > 75, lack of evidence for efficacy and safety in individuals with GFR < 30 ml/min
- Use with caution in elderly aged > 75 and GFR < 30 ml/min
Good Palliative-Geriatric Practice algorithm

- Consensus based flow chart
- For nursing homes
- Using this flow chart in study, 119 pts in intervention group and 71 patients in control
At the end of 1 year

- An average of 2.8 drugs per patients was discontinued
- Drug discontinuation failure was 18%
- 1 year mortality rate was 21% in the intervention group and 45% in the control group
- Hospital readmission rate was 11.8% of the intervention group, compared with 30% of the control group
- Decrease in the cost of drugs ($US 69 dollars per patient)
Case 2

- F/79, daytime alone
- HT, dementia and OA knee
- Witnessed syncope shortly after having dinner
- No chest pain or SOB or post-ictal drowsiness
- Medications: Amlodipine 5mg daily, exelon patch 9.6mg Q24H, panadol 500mg qid prn
• PE showed BP 134/76 P52 (supine), BP 128/72 P54 (standing)

• No heart murmur, no carotid bruit, no focal neurological sign, H’stix normal

• ECG showed sinus bradycardia, 40/min

• Holter showed min HR 35/min, RR 2.2 sec

• CT brain was unremarkable
Cholinesterase inhibitors & bradycardia

- ChEI (donepezil, galantamine & rivastigmine): RR bradycardia 1.4
- Dose effect: donepezil >10mg, 2.1 risk
- Clinical significance: ChEI use associated with:
  - Syncope: RR 1.76 (95% CI, 1.57-1.98)
  - Pacemaker placement: 1.49
  - Hip #: 1.18 (95% CI, 1.03-1.34)

Arch Intern med 2009;165:867
Progress

• She was noted to have 3 exelon patches stuck on different areas of her body
• Drug was administered by herself
• Relatives were instructed to put on a new patch only after the old patch was removed
• And write down the date on the new patch while applying.
Drug Counselling

• Actively offer counseling to elderly patients
  *BUT* .....  

• Make sure written materials are in a type font large enough to be ready

• For metered dose products, transdermal patches & other unique devices, *SHOW*, dont just tell, the patient how to use *BUT* ...

• For topical ointments & cream, demonstrate how to apply *BUT* ...
Drug Counselling

• Try to let the pharmacist to answer their questions / instruct how to take medications

Most elders greatly appreciate the care and attention regarding the Rx use

• If the patient is getting refills beyond the expected date, ask about the delay. May uncover problems with understanding or memory

• Home visit & education to caregivers will definitely avoid wrong drug administration & improve drug compliance
So how about in demented patients?

- Different medication organizers, pill boxes, phone & postal reminders have been studied in elderly patients’ drug adherence
- But the results were controversial
- Unfortunately NO study has been evaluated specifically in patients with dementia

Case 3

- M/78, ex-smoker, lives with wife, allergic to penicillin
- Hx of COPD on 1 liter LTOT, hypertension
- Ventolin puffs 2 qid
- Atrovent puffs 2 qid
- Becloforte puff 2 bd
- NuelinSR 200mg bd
- Norvasc 5mg daily
- Admitted for COPD infective exacerbation
- Low grade fever
- Develop vomiting, fast AF, restless & tremor on D3

- CXR showed no consolidation

- Cr 120 > 160 TSH normal

- Put on amiodarone infusion for fast AF

- Generalized tonic convulsion on D4

- BP 90/45 P114, rhonchi bilateral & was intubated

- And then toke over to ICU for further care
• **Theophylline level 48mg/L** (ref: 10-20mg/L)

• Seizure managed with midazolam & phenobarbitone

• And had hemoperfusion in ICU
Cytochrome P450 Drug-drug Interaction

- Case series showed 2x increased risk for theophylline toxicity with recent use of ciprofloxacin in elderly patient treated with theophylline (*Antonio et al 2011*).

- Theophylline is extensively metabolized in the liver by cytochrome P450 isoenzymes.

- Unlike other quinolones, ciprofloxacin appears to inhibit the CyP 1A2-mediated metabolism of theophylline, resulting in elevated theophylline concentration.

- Other Rx i.e. Erythromycin, amiodarone, Klacid clarithromycin, amdioarone.
<table>
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<th>CYP1A2</th>
<th>CYP2C19</th>
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Theophylline Overdose

- Narrow therapeutic range 10-20 mg/L
- SE are related to adenosine antagonism & catecholamine release and are dose dependent
- Mortality from arrhythmia & intractable seizure

Specific treatment: seizure can aborted by benzodiazepine, phenobarbitone (loading 20mg/kg over 30-60 minutes), phenytoin ineffective

- Haemoperfusion indication: I.O. , theophylline level 80mg/L (4x) or 40mg/L in elderly with severe S/S
Plasma level monitoring when prescribing for elders

- Digoxin
- Phenytoin
- Theophylline
- Valproic acid
- Amioglycosides
- Carbamazepine
Elders prone to theophylline overdose?

- Is it related to lower activity of cytochrome p450 in old age?
Cytochrome p450 activity in elders

- Microsomal cytochrome P450 dependent mono-oxygenase systems play a major role in drug & this capacity was reported to be diminished in aging

- A study in 2001 to assess the age-associated changes over time of plasma paraxanthine/caffeine (PAX/CAF) ratios used as a probe for CYP1A2 activity

- It DID NOT vary over time regardless of age, in vitro

But in vivo ....

- There are changes of pharmacokinetic and pharmacodynamic in elderly patients which will greatly affect the drug action i.e. decrease liver size & decrease liver blood flow, etc.
Pharmacodynamic

- Response that occurs when a drug interacts at its receptor

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pharmacodynamic effect</th>
<th>Age-related change</th>
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<tr>
<td>Adenosine</td>
<td>Heart-rate response</td>
<td>++</td>
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<tr>
<td>Diazepam</td>
<td>Sedation, postural sway</td>
<td>↑</td>
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<tr>
<td>Diltiazem</td>
<td>Acute and chronic antihypertensive effect</td>
<td>↑</td>
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<td></td>
<td>Acute PR interval prolongation</td>
<td>↓</td>
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<tr>
<td>Diphenhydramine</td>
<td>Postural sway</td>
<td>++</td>
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<tr>
<td>Enalapril</td>
<td>ACE inhibition</td>
<td>++</td>
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<td>Furosemide</td>
<td>Peak diuretic response</td>
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<tr>
<td>Heparin</td>
<td>Anticoagulant effect</td>
<td>++</td>
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<tr>
<td>Propranolol</td>
<td>Chronotropic effect</td>
<td>↓</td>
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</table>
Pharmacokinetics in Elderly

- Drug concentration at the site of action
Pharmacokinetic Changes with Aging

• Absorption
  • Gastric pH
  • Gastric emptying
  • Splanchnic blood flow
  • Intestinal motility
• Minimal clinical importance
Pharmacokinetic Changes with Aging

- Distribution
- Fat mass
- Muscle mass
- Total body water
- Albumin (binds acidic drugs e.g. Naproxen, phenytoin & warfarin)
- Alpha-1 glycoprotein (binds basic drugs e.g. Lidocaine, quinidine, imipramine & propanolol)

Clinically important
Effects of Aging on Volume of Distribution VD

- Body water > lower VD for hydrophilic drug (drug conc of ethanol, digoxin, levodopa & morphine)

- Lean body mass > lower VD for drugs that bind to muscle (plasma conc of digoxin)

- Fat stores > higher VD for lipophilic drugs (thiopental, amitriptyline, diazepam & tolbutamide)

- Plasma protein (albumin) > higher percentage of drug that is unbound (active)
Pharmacokinetic Changes with Aging

- Metabolism
  - Hepatic mass
  - Hepatic blood flow
  - First pass metabolism

- Clinical importance - marginal

- Cytochrome p450 activity remains unchanged in elderly
Pharmacokinetic Changes with Aging

- **Elimination**
  - Renal mass, renal blood flow
  - Glomerular filtration rate (10cc/decade)
  - **Most clinical important**
- Concentration of drugs dependent on renal clearance

- Serum creatinine alone does not provide adequate information to guide dosing
Case 4

- F/76, lives with family, ADL independent
- HT on Natrilix FU in GOP
- Depression since 2007, on amitriptyline 25mg nocte, FU in psychiatry
- PHx of L wrist and L hip # with DHS done
- Recently admitted with UTI, one month ago
• Readmitted for UTI again, complicated by delirium

• Significant PVR, put on Foley

• HypoNa 120

• Then transferred for Geri rehabilitation
Case 4

- Problems
- 1) Recurrent UTI
- 2) Fracture & Fall
- 3) Delirium

- Progress
- 1) Stopped amitriptyline
Amitriptyline

• Inhibits NE & serotonin re-uptake

• Metabolized extensively by liver CyP450 1A2, 2D6, 3A4

• Excreted by kidney

• Half life 10-26 hr; Half life of nortriptyline (its active metabolite) 18-44 hr

• Side effects:

• 1) Anticholinergic S/E i.e. Dry mouth, confusion, ROU, blurred vision, etc
Beers Criteria for Potentially Inappropriate Medication Use in older adult

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<td>TCA alone or in combination: Amitriptyline Clomipramine Doxepin &gt;6mg/d Imipramine Trimipramine</td>
<td>Highly anticholinergic, sedating and cause orthostatic hypotension; safety profile of low dose doxepin (&lt;6mg/d) is comparable with that of placebo</td>
<td>Avoid</td>
<td>High</td>
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</table>

Amitriptyline is rarely the antidepressant of choice for elderly patients
Bring Home Message

• Pay attention to polypharmacy, inappropriate drugs use for elders, drug-drug interaction, change pharmacokinetic & pharmacodynamic

• All will help to achieve drug adherence & avoid doing harm to your elderly patients
Medication Complexity Index

• The following factors were considered when scoring the complexity:

• 1. The number of medications in the regimen (score of one)

• 2. The number of doses per day (each dose receives a score of one)

• 3. The additional directions that must be followed, including take as needed, take with meals, take before meals, take after meals, no dairy products (each score of one)

• 4. The mechanical actions necessary to administer the medications including alternating doses, eye drops, inhalation, injections, ointments/creams, patch, etc. (each mechanical instruction receives a score of one)
Looking Beyond Polypharmacy

Patient nonadherent to at least 1 drug were discharged with a higher average MRC score (33.3 with 7 drugs)

MRCI seen to be a valuable tool for quantifying medication regimen complexity in clinical and epidemiological studies

BUT cut-off points not a/v

And not yet commonly use
• Finger tip unit (FTU), applied worldwide

• The amount of ointment, cream (but NOT foam) from 5mm nozzle of tube

• 1 FTU = distal skin crease to distal tip of index finger

• 2 FTU is approximately equivalent to 1g

• 2FTU applied to 4 hand print (including fingers)

• In the original UK study, one FTU weighed 0.49g in men and 0.43g in women (Finlay AY, Edwards PH, Harding KG. “Fingertip unit” in dermatology. Lancet 1989; II, 155)