

SPECIFICITIES OF PHARMACOTHERAPY IN PATIENTS OF SENIOR AGE

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Why change prescription in geriatric medicine?

How to change prescription in geriatric medicine?

Drugs potentially unsuitable at senior age

Drug mistakes in geriatric medicine

Specific characteristics of old-age morbidity I

Organs lose their functional reserve

Lower adaptation to changes of both internal and external environment

Easy decompensation of organ functions and organism as a whole

Health state assessment is difficult – discrepancy between objective and subjective condition

Polymorbidity (concomitant diseases – unrelated; chain of causes:

Immobilisation → phlebotrombosis → pulmonary embolism → pressure sores, urinary incontinence → sepsis)

Specific characteristics of old-age morbidity II

Microsymptomatology – asymptomatology
no fever, leucocytosis, silent myocardial ischemia

Mono(oligo)symptomatology

tachyarrhythmia (thyrotoxicosis)

➤ Non-specific symptoms

fatigue, dysorexia, weight loss

Secondary affection syndromes

symptoms in other than the affected organ – the lowest reserve (brain – delirious state, kidneys)

Catenating of symptoms (cascade reaction)

Atypical drug reactions

Geriatric patient requires a complex approach + individualization of therapy

Age associated changes

Polymorbidity

Drug – drug, drug – disease interactions

Chronic pharmacotherapy – changes in efficacy and safety
with time, revision of medication every 6 months

Course and results of treatment –
– increased variability

Safety of treatment

Complications of pharmacotherapy at old age

Chronic diseases

Disability

Increase in post-medication reaction

Polypharmacy

Potentially inappropriate medicaments for elderly patients

Non-compliance

Change in pharmacokinetics

Change in pharmacodynamics

Most frequent AEs in elderly patients

Cardiovascular system – orthostatic hypotension, arrhythmia, syncopes, falls

Gastrointestinal system - diarrhea, constipation, sickness, vomiting

Central nervous system - sedation, delirium, confusion, depression, extrapyramidal symptoms

Compliance decreases with old age

Up to 60% of seniors do not take medications according to their doctor's recommendation

Pharmacological compliance decreases with the number of drugs used and limited self-sufficiency (impaired eyesight, memory, ability, thinking)

Social compliance - loneliness, isolation, poverty

10 most frequently taken drugs in seniors

(International study Shelter 2009 - 2011)

1. Laxatives 42%
2. Drugs for acid-related disorders 41%
3. Antiaggregatory drugs 38%
4. Benzodiazepines 36%
5. Antidepressants 36%
6. Diuretic stimulants 35%
7. Analgesics 34%
8. Antipsychotics 26%
9. ACE inhibitors 23%
10. β -blockers 23%

Polypharmacy

Concurrent use of multiple drugs in a risky combination or in excess (clinically unnecessary)

Usually 4 and more drugs

Increases with age and polymorbidity

Polypharmacy

- Drug reactions often qualify a state considered to be a manifestations of ageing:

imbalance
giddiness
falls
nervousness
incontinence

somnolence
tiredness
asomnia
malaise
depression
confusion



Some may be indicative of a psychiatric treatment
→ with psychotropic drugs

Inappropriate prescription (most frequent mistakes)

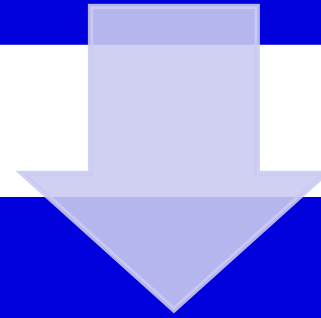
- Insufficient treatment (underprescribing)
Doctors do not prescribe drugs with demonstrable benefits (statins, antidepressants, ACEi)
- Redundant treatment with no indication (overprescribing)
Hypnotics, benzodiazepines, peripheral vascular dilators, nootropics
- "Imperative drugging"
A drug is prescribed for every single disease
- Prescription with a risk of interactions
- Prescription of high-risk profile medications
Drugs that are counter-indicated for comorbidities (β-blockers + COPD)

PHARMACOKINETICS at old age

Influenced by age-related changes

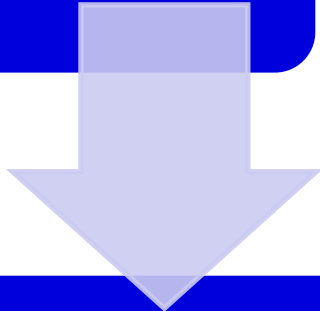
Age-related changes in drug pharmacokinetics and their clinical consequences - ABSORPTION

Decreased splanchnic and periphery perfusion,
Decreased GIT motility,
Absorption area decay (atrophy of mucosa and villi)
Increase in ventricle pH



Prolonged absorption after p.o. /i.m. administration
Delayed reactions to medications

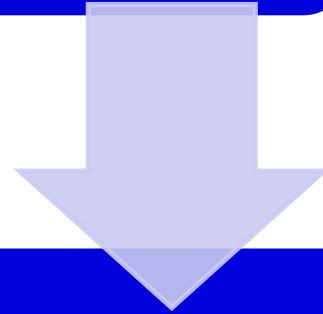
Age-related changes in drug pharmacokinetics and their clinical consequences - DISTRIBUTION

1. Decrease in total body water
 2. Increase in body fat
 3. Hypoalbuminemia
- 

1. Increase in plasmatic levels for hydrosoluble medicines (\downarrow **Vd**)
2. Risk of cumulation of liposoluble medicines – toxicity, prolonged elimination
3. Increase in free fraction of medicines with albumin linking (frequent malnutrition)

Age-related changes in drug pharmacokinetics and their clinical consequences - METABOLISM

Decrease in weight and liver perfusion
Decrease in CYP3A4 function
Decrease in glucuronidase in very old persons



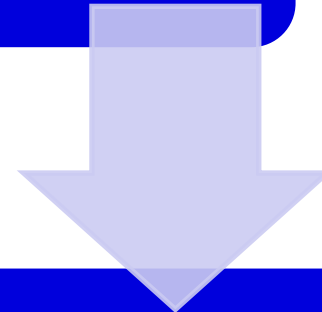
Slight slow-down in biotransformation
Increased risk of AE of drugs – drug interactions in polypharmacy

Age-related changes in drug pharmacokinetics and their clinical consequences – ELIMINATION

Decreased renal blood flow

Decreased glomerular filtration – physiological characteristic of old age

Decreased tubular secretion



Decreased excretion of drugs that are eliminated by kidneys

Prolonged T_{1/2} (amiodarone, digoxin, fluoxetine, alprazolam)

Danger of toxicity

PHARMACODYNAMICS at old age

Deterioration of homeostatic mechanisms

Changes cause an increased risk of adverse and unexpected reactions

Changes at receptor levels cause changes in tissue receptivity

Frequent clinical problems of seniors in relation to changes accompanying ageing:

Drugs with a negative impact I

Orthostatic hypotension (centrally effective antihypertensives, diuretics, β -blockers, tricycl. antidepressants, benzodiazepines)

Postural instability (same drugs as with ort. hypotension)

Extrapyramidal symptoms, dyskinesia (metoclopramide, classic antipsychotics, haloperidol)

Decrease in cognitive functions, behavioural disorders, delirium (centr. sympatholytics, tricyclic antidepressants, barbiturates, benzodiaz., analgesics-anodynes, antiparkinsonian agents, antihistaminics, H₂-blockers, theophylline, digoxin, indometacin)

Frequent clinical problems of seniors in relation to changes accompanying ageing:

Drugs with a negative impact II

Constipation, subileus (anodynes, tricycl. antidepressants, antihistaminics, spasmolytics)

Urinary incontinence (diuretics – loop, anticholinergics)

Increased risk of hypothermia (sedatives, hypnotics, antipsychotics, vasodilators, myorelaxants)

Risk of hyponatremia, susceptibility to dehydration (chlorpropamide, diuretics, SSRI)

Susceptibility to erectile dysfunction, gynaecomastia (α 1-sympatholytics, sedatives, urogenital tract spasmolytics, spironolactone, digoxin)

Frequent clinical problems of seniors in relation to changes accompanying ageing:

Drugs with a negative impact III

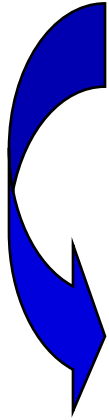
Increased risk of bleeding (increased sensitivity to warfarin, heparin)

Increased sensitivity to digoxine – AE already at therapeutical concentrations

Mark H. Beers, 54, Expert on Drugs Given to Elderly, Dies Feb 28, 2009

Beers' List

— Potentially Inappropriate
Medications for the Elderly



It is not about contraindications at administration, however utmost care is required!!!

Fick 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;163:2716-2724

New Beers' criteria (modified) 2012, 2015!!!

BEERS' LIST – for instance:

Medicament/drug group	Note, risks
Tricyclic antidepressants	Significant anticholinergic effect, risk of sedation, orthostatic hypotension and arrhythmias. SSRI are a safer alternative.
Barbiturates (nowadays obsolete)	Significant sedation, habit-forming, especially those with short-term effect are inappropriate.
Benzodiazepines	Risk of sedation, habit-forming, drugs with a long half-life are inappropriate (diazepam, flurazepam, chlordiazepoxid); benzodiazepine (oxazepam) with a short-term effect is more suitable, or nowadays these are not recommended at all!

General PRINCIPLES of pharmacotherapy in geriatric medicine

Know the effects of changes caused by ageing on the effect of medicines

Try to contribute to optimization of compliance (adherence)

Know the drugs that are better to be avoided in geriatric medicine

Know the **7 fundamental principles** of prescribing drugs in geriatric medicine

„Start low, go slow.“

„Start with a low dose and
increase it
slowly.“

Seven main principles of drug prescription in geriatric medicine

Remember a drug can cause a pathological symptomatology (disease)

Seek for establishing the diagnosis prior to prescription

Know the pharmacology of the prescribed drug well

Start „low" and proceed slowly; better still: start „low" and stay „low“

Be aware of other medications of the patient

Be careful about compliance

Regularly check the list of drugs taken

How to change prescription in geriatric medicine?

Adverse drug interactions

- Drug – drug interaction:

warfarin + sulfonamide (competition for a linkage to plasm. proteins)

alprazolam + zolpidem (drugs of the same group, potentiation of reaction)

anticholinergics + drugs with a high absorption capacity, antacids (slowed resorbence)

- Drug - disease interaction:

verapamil + impulse transfer disorder (heart rhythm disorder)

opiates, anticholinergics + dementia (delirium)

- Drug – food

grapefruit juice (CYP3A4 inhibitor)

herbaceous vegetables (vit. K – decreases the effect of warfarin)

chinolons + minerals (decreased absorption of chinolons)

Expert recommendations for geriatric pharmacotherapy

Expert consensus for the CR 2012

Recommended approach: Geriatric medicine for general practitioners 2010

Beers' criteria of 2003 (USA)

Laroche 2007 (France)

STOPP/START 2008 (Ireland) take into account (in)appropriateness of drugs at simultaneous assessment of patient's chronic diseases

New Beers' criteria 2012

Potentially inappropriate medications at old age

PIMs – potentially inappropriate medications
- the term coined by Beers in 1991 (USA)

= Drugs the potential risk in seniors over 65 overtops expected benefit at long-term treatment, or the efficacy of the medication is inadequate or inadequately verified

Indication unsupported with scientific evidence
Higher risk of post-drug reactions
Low cost effectiveness
A safer alternative is available in the market

STOPP and START criteria (Ireland 2008)

Listed according to physiological systems

STOPP criteria – e.g. cardiovascular system

digoxin – dosed 0.125 mg/day on a long-term basis in decreased kidney function ($Kr/S > 150 \mu\text{mol/l}$ and $\text{GF} < 50\text{ml/min}$)

loop diuretics with oedemas without signs of heart failure (unverified efficacy; suitable compression of extremities)

loop diuretics in monotherapy treating hypertension (safer and more efficient alternatives)

thiazide diuretics with gout (danger of causing an attack)

non-CS β -blockers with COPD (risk of bronchospasm)

diltiazem or verapamil with heart failure NYHA III-IV (risk of retrogression)

Ca channel blockers with chronic constipation

ASA + warfarin without protection against GIT bleeding (H_2 antagonists, proton pump inhibitors)

dipyridamol in secondary prevention of CVS in monotherapy

ASA dosed $> 150 \text{ mg/day}$ (unsubstantiated efficacy)

ASA with missing history or symptoms of IHD

warfarin unsubstantiated benefit of treatment longer than 6 months with uncomplicated deep vein thrombosis)

STOPP – patients with a history of falls

benzodiazepines

antipsychotic drugs

1st gen. antihistamine drugs

vasodilators

opioids

STOPP – analgesics

Strong opioids (morphine, fentanyl)

Long-term use of opioids (longer than 3 months), if laxatives are not used simultaneously, there is a risk of worsening cognitive deficits (exception: palliative therapy, severe chronic pain)