Fact Sheet: Basics of Old Age Psychopharmacology

Last updated Febrary 2024

Introduction:
Older adults undergo substantial changes in drug metabolism and elimination.

Cytochrome P450 System:
- Aging leads to slowed metabolism via the CYP system. This especially impacts the CYP1A2 and CYP3A enzymes but not CYP2D6, which has more resilience to the aging process.
- *Implication:* Elevated blood levels of numerous psychotropic drugs metabolized by the CYPA enzymes.
- Impacted agents include:
    - Antipsychotics (aripiprazole, clozapine, lurasidone, quetiapine, and ziprasidone).
    - Benzodiazepines (excluding lorazepam, oxazepam, temazepam).
    - Others: carbamazepine, buspirone, methadone, and trazodone.
- *Recommendation:* Prescribe smaller doses of medications metabolized by CYP1A2 and CYP3A3/4 and increase doses more slowly.

Fat Solubility and Accumulation:
There are increased fat stores in later life. Most psychotropics are fat-soluble.
- *Implication:* Psychotropics will be absorbed extensively into fat cells, where they are then stored, leading to their slow release and with time an increased risk of drug toxicity.
- *Impacted agents include:* Some of the most prominently impacted medications are benzodiazepines, clozapine, fluoxetine, haloperidol, olanzapine.
    - *Recommendation:* Prescribe smaller doses more frequently rather than larger doses less frequently.

Water-Soluble Drugs and Kidney Function:
Aging results in decreased body water and reduced kidney clearance of drugs.
- *Implications*: Medications that are water-soluble will have higher circulating concentrations, increasing the risk of drug toxicity.
- Impacted drugs: lithium, desvenlafaxine, gabapentin, paliperidone, pregabalin.
    - *Recommendation:* Increase doses of water-soluble medications slowly, target smaller doses, and lengthen dosing intervals. For lithium: target doses for older adults are 30% lower than for younger adults.

Other Important Tips for Prescribing in Older Adults:
- *Antipsychotics:* Boxed warning for increased risk of stroke and death in dementia. Monitor for increased QTc intervals.
- *Parkinson's Disease:* Antipsychotics may counteract levodopa/dopamine agonist effects, contributing to bradykinesia. Exceptions include drugs with low or no dopamine D2 receptor binding activity. These include clozapine, lumateperone, pimavanserin, and quetiapine. These agents are used preferentially to treat psychosis in patients with Parkinson's disease, though only pimavanserin is FDA-approved for this indication.
- *Tardive Dyskinesia:* Doubled risk in older adults; clozapine has lower risk, others debatable.
- *Orthostatic Hypotension:* Can contribute to falls and ischemic strokes. High risk with certain drugs.
- *Anticholinergics:*

    - Caution due to worsening cognitive impairment.
    - Avoid medications with strong anticholinergic properties when possible in OAs, including chlorpromazine, clomipramine, clozapine, desipramine, diphenhydramine, doxepin (>6 mg/day), hydroxyzine, nortriptyline, olanzapine, paroxetine, and perphenazine (AGS Beers Criteria®, J Am Geriatr Soc 2023;71(7):2052-2081).
- *Hyponatremia:* Increased risk with SSRI's/SNRI's, carbamazepine, oxcarbazepine.

General Recommendations:

- Due to slowed drug metabolism and elimination with aging, ***start low and go slow*** when starting and titrating medications, **but keep going** as many OAs will respond to the same final doses as younger adults.
- For most medications, start at one-half the usual dose and increase to the minimal effective dose after 1-2 weeks.
- Avoid making more than one medication change at a time.
- Minimize and simplify drug regimens when possible.
- Be cautious with agents that may cause orthostatic hypotension, daytime sedation, cardiac arrhythmias, or are anticholinergic.