The Geriatric Population and Psychiatric Medication

REZA NAGHDI MD
ASSIST. PROF. OF PSYCHIATRY
FELLOW IN DEMENTIA
TABRIZ UNIVERSITY OF MEDICAL SCIENCES

- Standards of medical care have been improving for the last 50 or so years throughout the world. This has led to an increase in life expectancy of the population causing a surge in the size of the geriatric subgroup.
- By 1990, a clear majority (58%) of the world's population aged 60 years and over was already to be found living in developing countries. By 2020 this proportion will have risen to 67%.

- Over this period of 30 years, this oldest sector of the population will have increased in number by 200% in developing countries as compared to 68% in the developed world (Murray & Lopez, 1996).
- Arrangements will have to be made to cater to the health needs of this ever-increasing subset of population.

hurdles in the provision of good mental health care to the elderly

- The presentation of psychiatric and physical illnesses may be different in the elderly as compared to the younger people.
- Some psychiatric symptoms like memory disturbances, depression and anxiety might be considered part of a normal aging process, which they are not.
- Training in geriatric psychiatry is limited, and this limits the availability of quality mental health care for the elderly population.
- Many health care professionals find it difficult to work with the elderly.

Pharmacokinetic Changes with Age

- Absorption
  - decrease in gastric acidity,
  - delay in gastric emptying,
  - decreased splanchnic blood flow and
  - decreased intestinal motility with age.
  - This results in slow absorption of drugs and a delay in their onset of action

- Metabolism
  - decrease in the hepatic mass,
  - decreased hepatic blood flow and
  - decreased in certain methods of metabolism as compared to others.
  - Hydroxylation and demethylation are examples of the latter, decrease in which leads to greater half-lives, prolonged action and accumulation of drugs such as diazepam and chlordiazepoxide
    - However, glucuronide conjugation remains unaffected by age, making drugs such as lorazepam and oxazepam safer in the elderly

- P-450 CYP2D6 activity does not change with age but its inhibition by various psychiatric or non-psychiatric drugs can alter the effect of other psychotropics.
- Drugs like fluoxetine, paroxetine, venlafaxine, mirtazapine and valproate inhibit P450 CYP2D6, which affects metabolism of drugs like desipramine, nortriptyline (TCAs), paroxetine, venlafaxine, carbamazepine, risperidone, clozapine, olanzapine and typical antipsychotics.
- This may cause complications in treatment of psychiatric disorders which might involve co-administration of these medications.

- **Excretion**
  - There is a loss of renal mass,
  - loss of glomeruli,
  - thickening of the basement membrane of the glomeruli and the tubules,
  - intimal thickening of the arterioles,
  - obliteration of the arterioles in the cortical glomeruli
  - These changes result in reduced glomerular filtration rate (GFR).
  - there is approximately 8.7 ml/min/1.73m^2 reduction in GFR per decade between the ages of 21–67 years.

- **Distribution**
  - an increase in the percentage of body fat in the body resulting in an increase in elimination half-life of many psychotropic medications.
  - a decrease in the total body water with age resulting in decreased volume of distribution of lithium and increase in its concentration
  - Less amount of plasma albumin in the elderly means a greater percentage of drug remains free in the blood which may result in higher incidence of adverse drug reactions.
  - Decreased cerebral blood flow results in decreased availability of drugs to brain for action at a particular serum concentration.

Pharmacodynamic Changes with age

- The sensitivity of Gaba-aminergic system is known to increase with age which results in a heightened response to drugs such as benzodiazapines (Greenblatt et al., 1977).
- Due to age related decrease in the dopamine turnover, the elderly are at an increased risk of developing drug induce Parkinsonism (Miguez et al., 1999).
- Decreased cholinergic activity may result in an increased response to anticholinergic agents (Umegaki et al., 2000).
- Serotonin reuptake and 5-HT2A receptor concentration decreases with age (Druse et al., 1997).

Benzodiazepines

- Because of the increased susceptibility to oversedation and memory and psychomotor impairment, elderly patients who take benzodiazepines are also more at risk for falls and skeletal fractures
- Long-term use (more than 30 days) of benzodiazepines is contraindicated in older adults due to risk of cognitive decline, poor functional autonomy, and addiction;
- Use of benzodiazepines as a sleep aid may actually worsen sleep patterns in older adults
- It is disturbing to note that 10% of geriatric hospitalizations are related to the use of benzodiazepines

- Hypnotic medications are prescribed for insomnia.
  - zolpidem, zaleplon, and eszopiclone
  - Mirtazapine, trazodone, nortriptyline, temazepam, and gabapentin

    all of which are often prescribed off label for insomnia

    may improve sleep quality in older adults,

    they generally are not recommended for long-term use
  - Sedating antihistamine drugs should be avoided, as they may be associated with delirium and other anticholinergic side effects.
- Prescribed hypnotic drugs should be tapered if taken for longer than 2 weeks

- Nursing Implications
- The use of benzodiazepines and hypnotic drugs should be avoided, or their use should not exceed 30 days, if possible
- When benzodiazepines are prescribed, it is preferable to avoid older drugs
  - diazepam
  - chlordiazepoxide

  which are more likely to accumulate and cause toxicity.

Antidepressants

- Antidepressant medications are prescribed for depressive disorders, anxiety disorders, and insomnia or depression with comorbid anxiety
- SSRIs, a newer generation of this class of medications, have become the preferred first-line treatment for depression in older adults

  as these drugs have more benign side effects than other antidepressant agents.
- Side effects common to SSRIs include headache, gastrointestinal disturbances, increased sweating, and sexual dysfunction.

- Tricyclic antidepressant drugs (TCAs), have a number of side effects that increase elderly patients' risk for falls.
  - sedation
  - psychomotor retardation
  - postural hypotension
  - anticholinergic effects, which may cause blurred vision and cognitive impairment.

  Fall risk is the greatest during the first 90 days of treatment, when dosages are being adjusted and before physiological adjustment has taken place

Nursing Implications

- When administering antidepressant drugs to older adults, nurses should be familiar with the drug category and the side effects most commonly associated with them.
- With use of TCAs and SSRIs, fall risk should be of greatest concern.
- Recognizing depression in older adults can often be challenging due to atypical symptoms.

Antipsychotics

- Antipsychotic medications, are also frequently administered to manage disruptive behavior in older adults with cognitive impairment.
- Typical antipsychotic medications (e.g., haloperidol) have several serious adverse effects that can affect quality of life, including
  1. tardive dyskinesia
  2. acute extrapyramidal side effects (EPSEs)
  3. neuroleptic malignant syndrome (NMS)
- Older adults are more at risk for these side effects than are younger patients
- Tardive dyskinesia involves abnormal muscle movements in the face, eyes, mouth, tongue, and limbs and can develop in 30% to 50% of patients, even at low drug dosages for short periods of time.

- EPSEs include
  1. drug-induced parkinsonism
  2. akinesia
  3. dystonia
  4. Akathisia
- Parkinsonism and akinesia consist of lack of or slowed movement, depressed affect, salivation, expressionless face, tremor, and shuffling gait.
- Dystonia is characterized by muscle rigidity, contracted neck and eye muscles, and jaw and muscle soreness. Dystonic reactions are less common in older adults for reasons that remain uncertain

- Akathisia is characterized by pacing and restlessness.
- Between 50% and 75% of all patients taking typical antipsychotic drugs experience EPSEs
- however, elderly patients are at higher risk for drug-induced parkinsonism and are at increased risk for EPSEs than are younger patients

- NMS involves:
  1. high fever
  2. rigidity
  3. altered consciousness
  4. autonomic system instability (i.e., unstable hypertension, tachycardia, sweating, pallor).
- NMS can be potentially fatal if not recognized and treated.
- Conditions such as neurological illness, dehydration, malnutrition, exhaustion, agitation, and organic brain disease are considered risk factors that make older adults more vulnerable to the development of NMS (Kidder, 1999).

- In addition to the previously stated adverse effects, older adults are more susceptible to the :
  1. anticholinergic (dry mouth, constipation, blurred vision, urinary retention) and
  2. cardiovascular (hypotension, cardiac conduction delay)

  effects of typical antipsychotic drugs

- Atypical antipsychotic medications (e.g., olanzapine [Zyprexa®], quetiapine [Seroquel®]) generally produce fewer of the adverse effects commonly associated with the typical antipsychotic medications.
- Weight gain is common, especially with clozapine (Clozaril®) and olanzapine (Boyd, 2008).

- On the basis of controlled studies of their use in younger patients, atypical antipsychotic drugs were initially considered a safer alternative in treating older adults with psychotic symptoms or agitation associated with dementia.
- However, recent warnings from the U.S. Food and Drug Administration (FDA) have emerged regarding the use of these medications with older adults due to cardiac, cerebrovascular, and mortality risks associated with their use in patients with dementia.

- A number of recent publications have called into question the common practice of administering atypical antipsychotic medications to patients with Alzheimer's disease.
- Much of the data regarding use of atypical antipsychotic medications with older adults remained unpublished by pharmaceutical companies, and thus the risk of untoward events from the use of antipsychotic medications was not widely known.

- A systematic review of published and unpublished literature on the use of atypical antipsychotic medications in patients with Alzheimer's disease revealed a number of dangerous side effects, including
  1. cerebrovascular events
  2. EPSEs
  3. somnolence
  4. upper respiratory tract infections
  5. edema, urinary tract infections
  6. fever

- *In 2005, the FDA completed a meta-analysis of clinical studies examining the use of atypical antipsychotic medications in patients with dementia.*
- *Results revealed a high death rate in patients who received atypical antipsychotic medications versus those treated with placebo.*
- *As a result, the FDA instructed drug manufacturers to add a black box warning to atypical antipsychotic drug labels indicating associated risks and that these drugs are not approved for use in patients with dementia (Jones, 2006).*

- A recent report from the Clinical Antipsychotic Trials in Intervention Effectiveness—Alzheimer's Disease (CATIE-AD) study revealed that

  the adverse effects of atypical antipsychotic drugs outweighed the advantages of these medications when administered to elderly clients with Alzheimer's disease

  Although the effectiveness of atypical antipsychotic drugs was greater than placebo, the adverse effects were found to limit their overall effectiveness.

  As a result, findings from this National Institutes of Health-sponsored study suggest that there is no clinical benefit of treatment with atypical antipsychotic drugs in patients with Alzheimer's disease.

Nursing Implications

- Nurses should monitor for
  1. oversedation
  2. orthostatic hypotension
  3. unsteadiness
  4. EPSEs

  when administering both typical and atypical antipsychotic drugs.
- To assess for tardive dyskinesia, a standardized assessment instrument such as the ***Abnormal Involuntary Movement Scale*** is recommended before treatment at baseline and then 4 weeks, 8 weeks, and at least every 6 subsequent months after starting antipsychotic medications

Anti-dementia Drugs

Cholinesterase inhibitors

- Several cholinesterase inhibitors (tacrine, donepezil, rivastigmine, and galantamine) are available for treatment of the cognitive deficits of mild to moderate Alzheimer's disease. All of these agents increase central cholinergic neurotransmission by inhibiting breakdown of acetylcholine by acetylcholinesterase.

- Tacrine- it is known to be hepatotoxic. Use is not recommended.

- Donepezil- most commonly used cholinesterase inhibitor. The main side-effects of donepezil include nausea, diarrhoea and insomnia.
- donepezil may help in depression and can exacerbate mania. Dose: 10 mg/day.

- Rivastigmine- more centrally acting cholinesterase inhibitor and is considered safe for hepatic function.
- Galantamine- it is a newer acetylcholine esterase inhibitor. Main side-effects of galantamine are nausea, vomiting, diarrhea, anorexia, weight loss, abdominal pain, dizziness and tremors

- Memantine

  Improvement in agitation and mood has been observed in several clinical trials, but cognitive and functional decline in Alzheimer's disease remains the main indication.

  Side effects are minimal, with dizziness, confusion, headache, and constipation being most often reported. Memantine undergoes little metabolism, and adverse drug-drug interactions have not been reported.

Thanks