MUNI
PHARM

Depression,
Anxiety, Sleep disorders in elderly

Depression

- Diagnosis complicated, can produce symptoms and signs of cognitive impairment, particularly in elderly patients
- Increased risk of dementia
- Patients with dementia may also present apathy, sleep impairment, and social withdrawal – indicating depression, but it is due to cognitive deficits
- Depression as a reaction OR direct biological consequence of neurologic disorder
- Depression is a major risk factor for suicide in older adults
- Depression is treatable

Risk factors for depression in elderly

Female sex
Social isolation
Widowed, divorced, or separated marital status
Lower socioeconomic status
Comorbid general medical conditions
Uncontrolled pain
Insomnia
Functional impairment
Cognitive impairment

- Recent onset of physical illness
- Greater severity of physical illness
- Functional disability and limited mobility
- Poorly treated pain
- Multiple illnesses

The Geriatric Depression Scale

5 items:

Are you basically satisfied with your life?

Do you often get bored?

Do you often feel helpless?

Do you prefer to stay at home rather than going out and doing new things?

Do you feel pretty worthless the way you are now?

Later-Life Depression Scales:

PHQ-9, Suicide Risk Checklist, and MoCA

Measurement-based care is critical for diagnosing major depression and the assessment of treatment efficacy and safety.
Symptoms of depression and cognitive function can be assessed with the PHQ-9 and MoCA

PHQ-9 (Patient Health Questionnaire-9) – MDCalc
MoCA - Cognitive Assessment (mocatest.org) Montreal Cognitive Assessment - highly sensitive tool for early detection of mild cognitive impairment (MCI)
Scores on rating scales can be monitored over time
Checking for risk and protective factors for suicide is critical

Depression in AD – diagnosis – criteria

The American Association for Geriatric Psychiatry

A. Three or more of the following symptoms, present during the same two-week period, and representing a change from a previous level of functioning. Either item-one or item-two must be included:

1. Clinically significant depressed mood
2. Decreased positive affect or pleasure in response to social contacts and usual activities
3. Social isolation or withdrawal
4. Disturbed appetite
5. Disturbed sleep
6. Psychomotor retardation or agitation
7. Irritability
8. Fatigue or loss of energy
9. Feelings of worthlessness, hopelessness, or inappropriate guilt
10. Recurrent thoughts of death or suicidal ideation, plan, or any attempt

B. Meets criteria for Alzheimer-type dementia

C. Depressive symptoms cause clinically significant distress or disruption in function

D. Symptoms do not occur exclusively during an episode of delirium

E. Symptoms are not due to a direct physiological effect from a substance (medication or drug of abuse)

F. Symptoms are not better accounted for by another condition

Dg. and treatment options

- Assessment for psychotic symptoms, hopelessness, insomnia, and malnutrition
- Medication(s) with depressant side effects (benzodiazepines, CNS depressants, opiates, other pain medications) or alcohol
- Treatment of other medical conditions commonly associated with depressive symptoms, particularly unrecognized thyroid disease, or diabetes, pain syndromes, malnutrition
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- Determination of personal history of prior depressive episodes, age of depression onset, prior drug therapy and outcome, and length of prior remission if achieved
- Determination of a family history of depression and family response to medication

The goal of treatment

Remission, Functional Recovery, and Prevention of Relapse and Recurrence of Later-Life Depression

Algorithm for Later-Life Depression Treatment: Antidepressants and Psychotherapy

- First-line pharmacotherapy in older adults with major depression consists of SSRIs, SNRIs, trazodone, mirtazapine, agomelatin, and bupropion.
- an appropriate dose of medication taken for a sufficient period is considered an adequate trial.
- Educate patients and their caregivers about the rationale for treatment and the importance of treatment adherence.

Pharmacotherapy

SSRI – choice of a specific drug based upon the side effect profile, drug interactions

Citalopram should not exceed 20 mg daily, should be avoided in patients at increased risk for arrhythmias

Sertraline among SSRI safe in CVS disorders, low drug interaction potential among SSRI

Paroxetine is the most anticholinergic of the SSRIs, risk of drug interactions

Fluoxetine has a long half-life and more drug interactions than other SSRIs, should be avoided

Other non-SSRI options: mirtazapine, trazodone, agomelatin, venlafaxine

Tricyclic antidepressants can cause confusion, cognitive impairment and other adverse effects

Adverse Effects of TCA

CVS – orthostatic hypotension, arytmia, cardiotoxicity

Anticholinergic – sedation, cognitive impairment, urine retention, obstipation..

Antihistamine activities

Adrenolytic effects

Proconvulsive effects

Sexual dysfunction

…

Pharmacotherapy

- side effect profiles, interaction potential - a major determinant in medication selection
- Monotherapy is preferred, augmentation for treatment-resistant older patients
- In elderly patients a full antidepressant response may not occur until 8 to 12 or even 16 weeks
- dosage should be adjusted for the older adult, typically the 1/2 usual starting dose for younger patients - to reach the same therapeutic dosage range as in younger adults
- monitoring esssential
- Duration - long-term treatment may be needed

Anxiety

Unpleasant state of tension or a fear that seems to arise from an unknown source, not related to a situational context, significantly affecting daily life X normal reaction to stress

Therapy of Anxiety

SSRI - are indicated to manage chronic anxiety or to treat mixed symptoms of anxiety and depression

Pregabaline – off label indication
structurally related to GABA, it does not bind to GABA or benzodiazepine receptors
inhibits excitatory neurotransmitter release

Hydroxyzin - acute anxiety
H1 antagonist – metabolite Cetirizine
Not inducing dependence, tolerance
AE: generally mild - drowsiness..
Interactions: CNS depressants

Guaifenesine
Anxiolytic and central muscle relaxant effects (200-2400mg), mild sedative eff., expectorans
Very low toxicity, OTC
AE: minimal – vertigo..
CI: myasthenia gravis, CNS depressants

Buspiron -generalized anxiety disorders, social fobia in combination, alcohol abuse, depression augmentation, switching from benzodiazepines
RISK in elderly:
CI: renal/hepatic dysfunction
Interaction: substrate CYP3A4 a 2D6,

Anxiolytic Drugs

Benzodiazepines

Differences: Duration of action, lipophilicity, affinity to its receptor

BZD long half-life
> 18 hrs
higher sedation
diazepam, chlordiazepoxid, medazepam, clobazam, clonazepam,

BZD intermediate half-life
12-18 hod
oxazepam, lorazepam, bromazepam, alprazolam, temazepam,

BZD short half-life
< 12 hod.
Do not cumulate in org
tofizopam, midazolam, triazolam

Metabolism: CYP450, glucuronidisation

Anxiety treatment

Benzodiazepines

Basic Principles:
NO : High doses, longterm treatment, unclear indication, fast discontinuation

CI: hypersensitivity, myasthenia gravis, alcohol intoxication, substance abuse,
sleep apnoa, glaucoma, renal and hepatic dysfunction, gravidity, lactation,

Adverse Effects:

drowsiness
ataxia, confusion, vertigo
amnesia, cogitive function impairment
paradoxical effects, such as agressivity, behavioral disinhibition
respiratory depression
hypotension
tolerance- to sedative, anticonvulsive, myorelaxant eff. NOT to anxiolytic, dependence
rebound and withdrawal phoenomena (2-10 days after, max. symtoms 5-15 days)
Confusion, Depersonalisation, delirium, tremor, seizures

Interactions:

e.g.

- Agents causing CNS depression
- Inhibitors of CYP3A4 - increase in plasma levels of triazolam, alprazolam, midazolam, diazepam, clonazepam

Benzodiazepines
use in elderly can cause

Sedation
Memory loss
Delirium
Confusion, particularly in patients with preexisting cognitive impairment
Gait instability
Paradoxical reactions

Benzodiazepine use in the elderly can lead to falls, hip fractures, and cognitive impairment

Sleep disorders

INSOMNIA:

1) **Initial**
2) **Impaired continuity**
3) **Terminal**

Causes of sleep disoders:

A) Primary – endogenous/exogenous

B) Secondary – somatic/ psychiatric disorders

Acute X Transitory X Chronic

1) **Transient – 1 night –** 1 week (stress reaction, jet lag syndrom)
2) **Short-term – 1-3 weeks (**psychosocial crisis, illness..)
3) **Long-term – more than 1 month** (somatic/psychic disorder, hospitalisation, age)

1.Parasomnia (talking, snoring...)

2.Hypersomnia

Sleep disorders

Common in elderly

in patients with AD - 25 to 35 percent of patients

age- and dementia-related changes in sleep and circadian rhythms, primary sleep disorders, comorbid illnesses..

Age-related changes –

- Total sleep time decreases by an average of approximately 30 minutes per decade starting in mid-life
- % of time spent in REM sleep decreases
- sleep phase advancement
- more fragmented sleep, decreased sleep efficiency, and increased daytime sleepiness
- changes in circadian rhythm - sleep-wake cycle
    - (eg, decreased rhythm amplitude and robustness, delayed rhythms)

Sleep disorders

Dementia-related changes - more disruptive sleep lower sleep quality and duration, imaired sleep architecture, circadian rhythm disturbances are more prominent

Causes are multifactorial:

- from depression and anxiety
- decrease in daytime physical activity
- nocturia
- side effects of medications

certain sleep disorders occur with increased prevalence in patients with certain types of dementia – e.g. restless legs syndrome..

Therapy

Nonpharmacologic treatment strategies are generally preferred

sleep hygiene

- An activity/exercise program
- increasing natural light exposure during the mornings
- limiting evening beverages, alcohol and coffee

Environmental restructuring

Management of polypharmacy

Stabilization and maintenance of consistent sleep-wake schedules

Stimulus control

Polypharmacy as a risk factor

excessive daytime sleepiness:

Benzodiazepines

Nonbenzodiazepine sedatives

Antipsychotics

Opioid analgesics

Beta blockers (lipophilic)

Barbiturates

Antihistamines

Anticonvulsants

Sedative antidepressants

Insomnia - Pharmacotherapy

HYPNOTICS

Mechanism of action: benzodiazepine rc GABA-rec. complex

I. Generation – obsolete (barbiturates/ clomethiasol, bromisoval, chloralhydrate)

II. Generation – Benzodiazepines - not for routine use

- midazolam (DORMICUM)
- triazolam

III. Generation - selective Ω1 benzodiazepine rec. agonists

- Zolpidem
- zopiclon

IV. Melatonin - Acts at receptors MT1, MT2 a MT3 - important role in regulation of circadian rhythms

V. Ramelteon, tasimelteon, - selective agonist of melatonin receptors MT_1 and MT_2

Agonism of MT_1 is thought to preferentially induce sleepiness, while MT_2 receptor activation preferentially influences regulation of circadian rhythms

VI. Orexin rcp antagonists – e.g. Suvorexant – blockade of orexin receptors, which is thought to supress wake drive, in elderly – may increase risk of somnolence, falls

Pharmacotherapy

NO role in the routine management of insomnia or other sleep-wake disturbances in patients with dementia

increased risk to a variety of side effects (eg, drowsiness, confusion, gait instability, nocturnal falls)

Melatonin - improve sleep maintenance and cognitive function
ramelteon
(agomelatin, trazodone, mirtazapine as antidepressants)

Insomnia- Conclusion
Principles of Treatment

1) Precise diagnosis – cause
2) Secondary insomnia – first prim. disease treatment
3) Low dose
4) No longer than 4 weeks regulary / 4-6 nights/month
5) Interactions
6) Informed patient – limitations, dependence

Deprescribing benzodiazepine receptor agonists Evidence-based clinical practice guideline

https://www.cfp.ca/content/64/5/339

Evidence-based guidelines recommend that deprescribing (tapering slowly) benzodiazepines be offered to elderly adults (≥ 65 years), regardless of duration of use. Deprescribing should be offered to adults aged 18-64 years who have used benzodiazepines for more than 4 weeks. These recommendations apply to patients who use these drugs to treat insomnia alone (primary insomnia) or comorbid insomnia where underlying comorbidities are effectively managed. This guideline does not apply to those with other sleep disorders (eg, restless leg syndrome) or untreated anxiety, depression, or other physical or mental health conditions that might be causing or aggravating insomnia.

The guidelines further state that tapering will help reduce withdrawal symptoms, although it may not eliminate them. At each step in the taper (approximately every 1-2 weeks), patients should be monitored for severity and frequency of adverse drug withdrawal symptoms, potential benefits, and mood, sleep quality, and changes in sleep. This can be done at a scheduled appointment or through a telephone call by a physician, psychologist, pharmacist, or nurse.

Herbs as Hypnotics

-Melissa off.

-Valeriana off.

-Humulus lupulus

-Crataegus monogyna

-Passiflora incarnata

-Hypericum perforatum

CONCLUSIONS

Behavioral and cognitive behavioral therapies offer very effective longer duration treatment and are recommended as first-line treatment options for insomnia compared to hypnotic medications in older adult

https://jcsm.aasm.org/doi/pdf/10.5664/jcsm.7172
Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia | The College of Family Physicians of Canada (cfp.ca)
https://www.cfp.ca/content/64/1/17?eto