Diagnosis and Management of Common Dementing Illnesses

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Prevalence

- Dementia in 49% of PACE participants
- Prevalence in NH population 50%
- Commonest dementias
  - Alzheimer’s 50 - 70%
  - Vascular 25%
  - Lewy body dementia 15%
Pre-dementia

- Mild cognitive impairment (MCI)
  - Measurable problem: memory, executive function, language, or visual spacial
  - Not causing significant impairment in independent living
  - Half of those with amnestic MCI stable for 3-5 years
Delirium

- Acute confusional state (acute brain failure)
- Confusion Assessment Method (CAM) of Inouye
- Patients with underlying dementia (chronic brain failure) are most susceptible
- It doesn’t respond to anti-cholinergic medicines
- A 2016 meta-analysis did not support anti-psychotic use.
- May not completely resolve
Diagnostic Methods

- History - possible causes, clinical course, function losses,
- Examination - particularly neurologic and psychologic
- Labs - Vit B12, TSH, CMET, RPR, chemistry panel, CBC
- Brain imaging - CT, but MRI is better
  - Atrophy - widening of sulci and ventricles - not diagnostic
  - T2 weighted image white-matter changes - not diagnostic
- Psychometric testing - MMSE, MoCA, SLUMS, Mini-Cog
- Investigational tests - rarely useful
Pre-dementia
Differentiating Dementing Illnesses

- Area of brain affected
  - Cortical - late onset of motor dysfunctions
  - Subcortical - early gait and bladder dysfunction
  - Diffuse - involves both areas

- Pathological changes
  - Amyloid plaques, neurofibrillary tangles
  - Lewy bodies
  - Vascular changes
Clinical Course

- Static vs progressive
  - Episodic
    - Sentinel event
      - Static encephalopathy - remains stable
      - Stair-step pattern - vascular events
    - Neurodegenerative - gradual loss of brain function
  - Improvement
    - Recovery from episode
    - Response to interventions and adjustments
    - Test variability
Cortical Dementias

- Alzheimer’s - Gradual decline in cognition
  - Early-onset Alzheimer’s - before age 65
- Fronto-temporal atrophy – early change in personality/behavior & loss of executive function
  - related aphasias
  - related disturbances of motor function
- Chronic traumatic encephalopathy
- Alcoholic encephalopathy
Alzheimer’s Dementia (AD)

- Most common - 60 - 70 %
- Increases with age - prevalence doubles every 5 years after age 65
- Brain pathology - amyloid plaques and neurofibrillary tangles
- Brain scans - hippocampal and/or medial temporal atrophy
- Inherited forms are rare and present earlier
Alzheimer’s Dementia (AD)

- Memory impairment is the cardinal initial symptom
  - Declarative episodic memory before semantic memory
  - Test with registration and recall
  - MMSE score below 25 = dementia (consider education)
    - Inexorable decline of about 3 points per year
    - Moderate dementia score 20 - 13
  - MoCA score below 26
  - Non-cognitive neurologic deficits come later
Natural History of Alzheimer

- Life expectancy of 6-10 years
- Mild - significant short-term memory problems, losing IADL’s
- Intermediate - losing ADL functions
- Severe - has lost all ADL functions
- End-stage - bed ridden, dysphagic
- Evidence that anti-oxidant Vitamin E slows progression
Subcortical and Diffuse

- Subcortical - vascular, Parkinson’s and normal pressure hydrocephalus
  - early neurologic deficits and gait changes
- Cortico-subcortical – Diffuse Lewy body
  - Parkinsonism, fluctuations, visual hallucinations and delusions
- Multifocal – Subacute spongiform encephalopathy (Prion disease, CJD)
  - rapid decline
Vascular Dementia (VaD)

- No uniform diagnostic criteria
- Pathology
  - Large artery infarcts - cortical and subcortical
  - Small artery infarcts (lacunes) - subcortical
  - Chronic subcortical ischemia (lipohyalinosis, microatheromata, cerebral amyloid angiopathy)
  - Mixed - 1/3 with VaD also have AD changes
Dementia with Lewy Bodies

- Parkinsonism
- Visual hallucinations
- Cognitive fluctuations
- Dysautonomia
- Sleep disorders
- Neuroleptic sensitivity
Potential Benefits of Treatments

- **Individual** – preservation of independence and normalcy
- **Family** – decrease care-giver burden and delay institutionalization
- **Institutions** – reduce demands on staff and ill-effects on other patients
- **Clinicians** – delay the need for interventions and the switch to comfort care
- **Society** – prolong productivity and decrease costs of care
Treatment Approach

- Determine type of dementia and stage
- Consider confounding factors
  - Co-morbidities
  - Functional effects
  - Family support
  - Economics
  - Life expectancy
  - Psychological and behavioral responses
- Trials of medications
Review Medications

- Remove those with anticholinergic effects
  - muscle relaxants, anti-spasmodics, OTC sedatives
- Decrease sedatives affecting daytime function
- Antipsychotics have a black box warning
- Schedule pain medications
- Review dosing timing and possible interactions
Dementia Treatments

- Historical – Pavabid, Hydergine
- Hormonal and Alternative Medicines
- Anticholinesterases
- N-methyl-d-aspartate receptor agonist - memantine
- Sedatives, mood stabilizers, anti-psychotics
- Meds to control hypertension, diabetes, and hyperlipidemia
- Antiplatelet and anticoagulants
Clinical Evidence

- Beneficial - Bold
- Likely to be Beneficial - Italic
- Weak evidence of benefit - plain
- (Ineffective) - in parenthesis
- {Evidence for harm}
- [Cost for 30 days of average dose, generic if available]
Prevention of Dementia

- Antioxidants - (Vitamin E)
- Vitamin D (Multivitamins, Vitamin B6 & B12, folate)
  - No benefit seen from lowering homocysteine
- Diet - Mediterranean, high fruits and vegetables, (omega-3 fatty acids)
- (Alcohol, NSAID’s, antiplatelet, estrogen replacement, Ginko Biloba)
- Healthy lifestyle, exercise
- Hypertension treatment, {statins, diabetes control}
Behavioral

- Reality orientation - improved behavior
- Aromatherapy, music therapy, exercise, care-giver training
- Multimodal - NH and ALF populations
  - Comprehensive training of nursing home staff improved behavior and lessened psychotropic use
  - (Nonpharmacologic care-delivery interventions)
  - Insufficient evidence of efficacy for agitation or aggression
Anti-depressants

✦ May be depressed before oblivious to their condition
✦ Low anti-cholinergic tricyclics, e.g., nortriptyline
  ✦ if side-effects useful, e.g., pain adjuvant, spasms
✦ Mirtazepine - if need sedation and appetite stimulation
  ✦ [$53 for 30 mg tab]
✦ SSRI - well tolerated by most, citalopram
  ✦ consider QT interval and arrhythmia risk
✦ SNRI - also help as pain adjuvants
Mood stabilizers & Anti-anxiety

- **Carbamazepine** - reduced agitation and aggression [$28]
- (Valproate) - helped agitation in one RTC, but didn’t help aggression in another
- (Trazadone) - no benefit in one trial
  - sedating without anti-cholinergic [$10 for 50 mg tab]
- {Benzodiazepines} - use short half-life drugs, if can’t control anxiety otherwise
- **Cholinesterase inhibitors** - modest beneficial effect
- (Memantine) - no clinically significant effect
Anti-psychotics

- If psychotic features otherwise uncontrollable
- All now have a black-box warning
- Use for delirium in hospitalized patients?
  - A 2016 meta-analysis did not support their use.
- A 2016 RCT of a multidisciplinary intervention in NH patients
  - provided staff with comprehensive behavior management training
  - improved demented patient’s behavior with less psychotropic medicine use
Anti-cholinesterases

- **Donepezil** - improved cognitive function and global clinical state in Alzheimers [$215]

- **Galantamine** - improved cognitive function and global clinical state up to 6 months [$132]

- **Rivastigmine** - improved cognitive function in AD and Lewy Body, but significant GI side-effects - 3 mg tab [$263], patch 13.3mg [$595]

- Delay decline in function about 6 months
Recommendations for Dementia Rx

- Give modest expectations for responses
- Mild-moderate – cholinesterase inhibitor
- Moderate-severe – add memantine
- Severe – trial off off cholinesterase inhibitor
- Delusions, hallucinations – quetiapine
- BP control - helps under age 80
- Statin and DM control - poor data
- Antiplatelet and homocysteine lowering - no benefit
DLB Treatment

- Donepezil helps in 10 mg dose
- Memantine has variable evidence of benefit
- Neuroleptics - catastrophic reactions - quetiapine if necessary
- Avoid benzodiazepines - paradoxical agitation
- For REM sleep disorder - melatonin
- Parkinsonism - levadopa - may respond poorly to all meds
- OH - fludrocortisone, midodrine
Treating Co-morbidities

- Anxiety/depression - familiar inputs, trazodone, SSRI, benzodiazepine
- Insomnia - trazodone, melatonin, benzodiazepine
- Pain - acetaminophen, narcotics, SNRI, lidoderm
- Appetite loss - mirtazepine, (Megace)
- Sexual aggression - SSRI
Conclusions

- Differentiating dementia types and co-morbidities guides treatment

- Our proven armamentarium for preventing and treating dementia is very limited

- Unwanted behaviors are best treated with behavioral approaches