Advances in Ambulatory Care for the Older Adult: An Evidence-Based Approach

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Objectives:

At the conclusion of this workshop the attendee will be able to:

1. Apply new evidence to effectively manage hypertension & diabetes in the elderly.
2. Summarize recent recommendations on calcium and vitamin D.
3. Describe the latest studies of diagnosing, treating, managing Alzheimer's disease.
4. Explain the results of studies that prompted the FDA warnings for anti-psychotic use in patients with dementia.
5. Describe the various diagnosis and treatment options for insomnia.
6. Identify & treat common non-pain symptoms at the end-of-life.
Mrs. Zheimer

- Mrs. Zheimer is an 80 year old woman with a history of memory problems, diabetes mellitus and hypertension

- She is here to establish primary care with you

- Her PMH is only significant for a myocardial infarction 4 years ago
Mrs. Zheimer

Her medications include:

Lisinopril 10mg daily
Metoprolol XL 50mg daily
Metformin 500mg twice daily
Atorvastatin 10mg nightly
Aspirin 81mg daily

Her blood pressure is 152/75
Hypertension

Considerations

What is the target blood pressure for Mrs. Zheimer?

What is the ideal treatment for hypertension in the elderly?

Is over treating blood pressure harmful?
# Hypertension – *JNC Classification*

Adults ≥ 18 years old

<table>
<thead>
<tr>
<th></th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal</strong></td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td><strong>Pre-hypertension</strong></td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td><strong>Stage 1 Hypertension</strong></td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td><strong>Stage 2 Hypertension</strong></td>
<td>≥ 160</td>
<td>≥ 100</td>
</tr>
</tbody>
</table>

Efficacy of HTN treatment in the elderly

<table>
<thead>
<tr>
<th>Event</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>0.66 (0.58-0.74)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.79 (0.69-0.90)</td>
</tr>
<tr>
<td>Cardiovascular Mortality</td>
<td>0.77 (0.68-0.96)</td>
</tr>
<tr>
<td>Any Cardiovascular event</td>
<td>0.72 (0.68-0.77)</td>
</tr>
<tr>
<td>All-cause Mortality</td>
<td>0.90 (0.84-0.97)</td>
</tr>
</tbody>
</table>

Hypertension in the elderly

- Various epidemiologic population studies have suggested improved survival with higher levels of blood pressure.

- Worse survival reported with SBP <140 mmHg (Oates et al. 2007).

- Meta-analysis (n=1670) [Lancet: Gueyffier et al. 1997 – INDANA]
  - 36% reduction in the risk of stroke [BENEFIT]
  - 14% increase in total mortality (p=0.05) [RISK]

- HYVET (Hypertension in the Very Elderly Trial) pilot results (n=1273) similar results to meta-analysis.
The Trial:
International, multi-centre, randomised double-blind placebo controlled

Inclusion Criteria:
- Aged 80 or more,
- Systolic BP: 160 - 199 mmHg
- + diastolic BP: < 110 mmHg,
- Informed consent

Exclusion Criteria:
- Standing SBP < 140 mmHg
- Stroke in last 6 months
- Dementia
- Need daily nursing care

Primary Endpoint:
All strokes (fatal and non-fatal)

Target blood pressure
150/80 mmHg
HYVET trial

- 30% reduction in all stroke (p=0.055) – consistent with HYVET pilot study and the INDANA meta-analysis
  - 21% reduction in total mortality (p=0.019)
  - 39% reduction in fatal stroke (o=0.046)
  - 64% reduction in heart failure (p<0.0001)
  - No reduction in dementia rates

NNT (2 years) = 94 for stroke
  = 40 for mortality
Mrs. Zheimer

- You examine Mrs. Zheimer and the only positive finding is that she is orthostatic.

- Her blood pressure on sitting is 152/75. However on standing, it drops to 120/60.
Orthostatic Hypotension

**Definition:** ≥ 20 mmHg fall in systolic pressure
≥ 10 mmHg fall in diastolic pressure

- Increases with age, HTN, certain drugs
- Associated with a higher risk of:
  - All cause mortality
  - CVS mortality
  - Stroke
  - CAD
  - Dementia
  - Falls & Fractures
Orthostatic Hypotension

- Only recognized in the Syst-Eur and HYVET trial

- HYVET trial suggested that if standing systolic BP <120 mmHg, do not try to treat the hypertension

- If considering medications changes, CHECK ORTHOSTATICS!
Can BP be too low?

**ONTARGET study** *(J Hypertens 27(7);1360-1369, 2009)*

- Systolic blood pressure <130
- Diastolic pressures <60-70

- Associated with higher rates of ischemic heart disease
- Not thought to affect stroke, in fact the opposite. Lower pressure, lower rates of stroke
Does treatment of Hypertension prevent dementia?

- Prior studies have shown mixed results

- SYST-EUR and PROGRESS suggest decreased incidence of stroke-related dementia with the use of an ACE-I (+/- diuretics) and reduced incidence with dihydropyridine calcium antagonists

- HYVET showed no reduction in dementia rates but the follow up was short (2 years)
### Hypertension and treatment

**Table 1. Classification and Management of Blood Pressure for Adults Aged 18 Years or Older**

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>Systolic BP, mm Hg*</th>
<th>Diastolic BP, mm Hg*</th>
<th>Lifestyle Modification</th>
<th>Initial Drug Therapy Without Compelling Indication</th>
<th>Initial Drug Therapy With Compelling Indications†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 and &lt;80</td>
<td></td>
<td>Encourage</td>
<td>No antihypertensive drug indicated</td>
<td>Drug(s) for the compelling indications‡</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139 or 80-89</td>
<td></td>
<td>Yes</td>
<td>Thiazide-type diuretics for most; may consider ACE inhibitor, ARB, β-blocker, CCB, or combination</td>
<td>Drug(s) for the compelling indications</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140-159 or 90-99</td>
<td></td>
<td>Yes</td>
<td>2-Drug combination for most (usually thiazide-type diuretic and ACE inhibitor or ARB or β-blocker or CCB)§</td>
<td>Drug(s) for the compelling indications</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160 or ≥100</td>
<td></td>
<td>Yes</td>
<td>2-Drug combination for most (usually thiazide-type diuretic and ACE inhibitor or ARB or β-blocker or CCB)§</td>
<td>Drug(s) for the compelling indications</td>
</tr>
</tbody>
</table>

**Management**

- **Without Compelling Indication**
- **With Compelling Indications†**

**Initial Drug Therapy**

- **Drug(s) for the compelling indications‡**
- **Drug(s) for the compelling indications**
- **Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, β-blocker, CCB) as needed**

**Abbreviations:**
- ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; BP, blood pressure; CCB, calcium channel blocker.

*High treatment determined by highest BP category.
†See Table 6.
‡Treat patients with chronic kidney disease or diabetes to BP goal of less than 130/80 mm Hg.
§Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

Chobanian et al. JAMA.2003. 289:2560-2572
JNC Algorithm for treatment for Hypertension

Chobanian et al. JAMA.2003. 289:2560-2572
# JNC Compelling indications for individual drug classes

<table>
<thead>
<tr>
<th>High-Risk Conditions With Compelling Indication*</th>
<th>Recommended Drugs</th>
<th>Clinical Trial Basis†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diuretic</td>
<td>β-Blocker</td>
</tr>
<tr>
<td>Heart failure</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Post–myocardial infarction</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>High coronary disease risk</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Diabetes</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Recurrent stroke prevention</td>
<td>•</td>
<td>•</td>
</tr>
</tbody>
</table>

*Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed in parallel with the blood pressure.

†Conditions for which clinical trials demonstrate benefit of specific classes of antihypertensive drugs.
Hypertension and treatment

- Achieving an optimal BP appears to be more important than specific drug selection.

- At least 5 classes of drugs provide benefit in reducing mortality (thiazide diuretic, ACE inhibitor, ARB, CCB, B-Blocker).

- Choose drug based on patient characteristics and other chronic conditions.
Mrs. Zheimer

- Given that she is a diabetic, we would like her BP to be <130/80. However since she is orthostatic, we will not try to achieve this goal.

- Her BP is well managed as we want to get it to as close as 150/80

- She is on a B-Blocker, ACE-inhibitor and ARB for his BP which is ideal for her chronic conditions of coronary artery disease and diabetes

- No medication changes needed for Mrs. Zheimer
Mrs. Zheimer

- You check Mrs. Zheimer’s labs and they are all within normal limits

- Her HbA1C is 7.4

Is this level acceptable for Mrs. Zheimer? Do we need to improve her glycemic control?
UKPDS trial

- Microvascular complications (retinopathy, nephropathy, neuropathy) decreased by 25% by achieving an HbA1C of 7
- Early control of diabetes led to better outcomes
- No effects seen on cardiovascular complications or mortality
ACCORD trial

- 10,251 patients randomized to either:
  - Intensive therapy: target HbA1C <6.0
  - Standard therapy: target HbA1C 7-7.9

- Mean age = 62 years

- Median HbA1C = 8.1
ACCORD trial

Tight glucose control with HbA1C <6 compared with an HbA1C 7-7.9 lead to:

- Increased mortality by 22%

- Did not significantly decrease major cardiovascular events

The Action to Control Cardiovascular Risk in Diabetes Study Group. NEJM 2008;10.1056
4700 high risk patients with type II diabetes were randomized to:
- intensive therapy: target systolic BP < 120 mmHg
- standard therapy: target systolic BP < 140 mmHg

Results:
- No difference in nonfatal MI, nonfatal stroke or cardiovascular death
- Increased complications from antihypertensive therapy
ACCORD trial – outcomes at 5 years

- Overall mortality remained significantly higher in the intensive-treatment group than in the standard group (7.6% vs. 6.4%).

- Intensive-treatment group had fewer nonfatal myocardial infarctions, a similar number of nonfatal strokes, and a higher incidence of cardiovascular death.

- For a primary composite endpoint that combined these three individual outcomes, no significant difference was noted between the intensive-treatment and standard-treatment groups.

- Within the intensive glucose-lowering group, patients who were also assigned to intensive blood pressure (BP)-lowering (systolic target <120 mm Hg) in a BP substudy experienced higher all-cause mortality than those assigned to a target BP of <140 mm Hg.
ADVANCE trial

- Multi-center, international RCT

- 12,877 patients randomized to either:
  - Intensive therapy: target HbA1C 6.5%
  - Standard therapy: target HbA1C 7.3%
  - Mean age: 66
  - Median HbA1C: 7.5
ADVANCE trial

Intensive treatment caused:

- No significant difference in the rate of death from any cause or cardiovascular cause
- No significant difference in the rate of major macrovascular events
- Decreased major microvascular events mainly a decrease in nephropathy
- No significant effect on retinopathy
- Severe hypoglycemia was more common

The ADVANCE Collaborative Group. NEJM 2008;10.1056
Cardiovascular safety of pioglitazone and rosiglitazone in older patients with Diabetes

- Rosiglitazone was thought to have an increased risk of MI and cardiovascular causes of borderline significance (NEJM 2007;356:2457-2471)

- In older patients with diabetes, pioglitazone instead of rosiglitazone was associated with a lower risk for:
  - composite death or admission for heart failure
  - MI
Mrs. Zheimer

- Given her HbA1C is 7.4, based on these trials, she has good diabetic control and doesn’t need to add any treatment for tighter control

- Also based on this, her blood pressure is acceptable and she doesn’t need to change her medication
Mrs. Zheimer

- It is two years later and you are seeing Mrs. Zheimer, who is now 82 years old, for a routine follow up visit.

- Her husband notes she’s been a little forgetful and recently he started taking over managing her medications.

- He notes that she is has been taking calcium with vitamin D for a long time, but he saw something recently in the news that calcium can cause heart attacks.

- Should she continue taking calcium with vitamin D and how much?
Why Take Calcium?

- Prevention and treatment of osteoporosis
- Calcium increases bone mineral density
- Meta-analyses have shown only modest benefit of supplementation with calcium alone or calcium with D in reducing fractures \(^1\)
- NNT for 5 years to prevent 1 fracture estimated to be 39-48
- Little evidence of health risk of supplementation
  - Slight increase risk of kidney stones

Vitamin D for Fall Prevention

- JAMA 2004 - 800 U/day ↓ odds of falling in elderly by 22%, NNT 15
- BMJ 2009 - 700-1000 U/day ↓ risk of falling by 19%. Serum 25(OH)D level ≥60 to be effective
- Cochrane 2009 - Vitamin D supplementation in those with low levels ↓ rate of falls by 43%
- JAGS 2010 – 200-1000 U/day results in 14% fewer falls

- Kalyani RR. JAGS 2010
Fall prevention by dose of vitamin D

Dose of vitamin D$_2$ or vitamin D$_3$ (IU)

Fall prevention by 25-hydroxyvitamin D$_3$ level

25-hydroxyvitamin D$_3$ serum concentration (nmol/l)
Calcium & Vit D and Heart Disease

- WHI – found no affect of calcium and vit d on CV outcomes or mortality
- Recent systematic review to assess whether vit D, calcium or both reduces risk of CV events
- 17 trials included – RCTS and prospective cohort studies
- Slight but non-significant reduction in CVD risk in patients taking vitamin D (1000 IU/d)
  - No difference in those receiving calcium alone or calcium and vitamin D

Calcium & Risk of MI

- Meta-analysis to evaluate if calcium supplementation increases risk of CV events
- 15 RCTS of calcium alone (≥ 500mg/d)
- Calcium supplementation associated with 30% increase in risk for MI
- Non-significant increase in stroke and mortality

- Treating 1000 pts w/ calcium for 5 years would result in 14 MI, 10 CVA, & 13 deaths, and prevent 26 fractures.

- Bolland, et al. BMJ July 2010
Dietary Calcium

- Risk of MI with calcium supplements was higher in those with greater dietary calcium intake
- Observational studies suggested higher dietary calcium was protective against CV disease
- CV risk from high calcium intake may be restricted to use of calcium supplements
- Safest thing may be to get calcium from good dietary sources to help fight OP without increasing CV risk
  - Skim milk, yogurt, sardines, fortified juices
IOM Nov 2010

- Most people don’t need calcium & vitamin D supplementation
- Daily calcium intake should be 1200mg for women 51 and older and men 71 and older
  - Most can achieve through diet alone but if have only 1-2 servings may need a supplement
- Vitamin D deficiency at <12 ng/ml, inadequate below 20 ng/ml
- Recommend 800 units daily for those 71 and older
Guidelines

- National Osteoporosis Foundation
  - Recommends 1200 mg calcium daily from diet and/or supplements for those >50 years
  - Vitamin D inadequate <30 ng/ml & recommend 800-1000 IU daily for those >50 years

- AGS
  - Recommends Vitamin D 800 IU daily for older adults
Take Home Points

- Obtain daily calcium requirements from food
- Calcium supplements for those with low dietary intake, always given with vitamin D
- Target those patients at increased risk for falls and fractures for treatment
- Vitamin D 800-1000 units per day
- May need more if levels not 20-30 ng/ml
Mrs. Zheimer

- She reports eating 1-2 servings of dairy products daily. Generally she has a yogurt and occasionally some cheese.
- You will have her continue Calcium with Vitamin D (600 mg-400 unit tab), but just one tablet once a day.
- Add additional vitamin D 400 units daily & check vitamin D 25,OH level with next labs.
"I remember the face but I've forgotten your name."
Mrs. Zheimer

Mrs. Zheimer is 85 years old. Mr. Zheimer tells you she has been forgetting names of some of her friends, misplaces things, and has trouble cooking some of her familiar dishes for dinner. He read about some new tests for Alzheimer's disease and wants you to order them.
Dementia Diagnosis

- In CSF: $\beta$-amyloid protein 1-42/phosphorylated tau$_{181P}$ biomarker mixture model identified 1 feature linked to AD, while the other matched the "healthy" status.

- AD signature found in 90% of patients in the AD group

- 68 autopsy-confirmed AD cases, 64 of 68 patients (94% sensitivity) were correctly classified with the AD feature.

- MCI patients (n = 57) followed up for 5 years: sensitivity of 100% in patients progressing to AD.

Two Tests Could Aid in Risk Assessment and Early Diagnosis of Alzheimer's

By GINA KOLATA
Published: January 18, 2011
Dementia Diagnosis

- Low $\beta$-amyloid 42/40 level was associated with greater cognitive decline (9-year 3MS)

- Results were similar after multivariate adjustment for age, race, education, diabetes, smoking, and apolipoprotein E [APOE] e4 status and after excluding the 72 participants with incident dementia.

Yaffe K, et al. JAMA. 2011;305(3):261-266:
Dementia Diagnosis

- Florbetapir-PET imaging prior to death

- 15/29 individuals (51.7%) met pathological criteria for Alzheimer disease.

- Florbetapir-PET images and postmortem results rated as positive or negative for β-amyloid agreed in 96% of the 29 individuals in the primary analysis cohort.

- The florbetapir-PET image was rated as amyloid negative in the 74 younger individuals in the nonautopsy cohort

Dementia Treatment

- RCT at 219 sites to test the effectiveness and tolerability of increasing donepezil from 10 to 23 mg/d in patients with moderate to severe AD.

- RESULTS:
  - LSM (SE) Delta in SIB score was significantly greater with donepezil 23 mg/d than with donepezil 10 mg/d ($P < 0.001$).
  - 30% drop-out rate in intervention vs. 17% in control
  - Common side effects at 23-mg/d dose were nausea, vomiting, diarrhea, dizziness

- In moderate to severe AD, donepezil 23 mg/d was associated with greater benefits in cognition compared with donepezil 10 mg/d.

Dementia Prevention: Exercise

- Metanalysis of 15 prospective studies (12 cohorts)
- 33,816 nondemented subjects followed for 1–12 years.
- 3,210 patients showed cognitive decline.
- Physical activity significantly protected (−38%) against cognitive decline during the follow-up ($P < 0.00001$).
- Low-to-moderate level exercise also showed a significant protection (−35%) against cognitive impairment ($P < 0.00001$).
- Suggests protection for all levels of physical activity against the occurrence of cognitive decline.

Dementia Prevention: Vitamin D?

- Low levels of vitamin D were associated with substantial cognitive decline in the elderly population studied over a 6-year period.
- Weekly dietary intake of vitamin D was associated with improved cognitive performance in older women.

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Mrs. Zheimer

- You perform office-based cognitive testing
- She is diagnosed with mild Alzheimer’s disease
- Your rx:
  - Begin Aricept at 5mg and increase to 10mg as maintenance dose
  - Encourage physical activity
  - Continue vitamin D 1000iu/day
- You do not perform:
  - Serum amyloid levels
  - Florbetapir-PET scan
Mrs. Zheimer

- Mrs. Zheimer is 87 years old. She is in the mild stages of Alzheimer’s disease.
- She is accompanied by her husband. In addition to her memory problems, she reports feeling depressed and anxious. Her husband agrees with this. She has eliminated many of her social activities.
- They are both looking for advice.
Depression

- 20-25% of patients with Alzheimers have depression
- Major cause of disability
- Poor quality of life
- More physical aggression
- Earlier nursing home placement
- Possibly higher mortality
Treating Depression in Alzheimer's Disease: The DIADS

- RPCT, outpatients, N=44
  - Using Sertraline to treat depression in patients with Alzheimer's disease
  - Outcome measure: ‘response to treatment’, depression, ADL impairment, behavioral disturbance, cognition, adverse effects

Arch Gen Psychiatry 2003
Results

- Treatment improved depressive symptoms
  - P=.007
  - Independent psychiatrists review of CSDD (Cornell Scale for Depression in dementia) and HDRS (Hamilton Depression Rating Scale)

- Responders to treatment showed trend toward less decline in activities of daily living, less behavioral disturbances, less caregiver stress
Mrs. Zheimer

- You perform a Geriatric Depression Scale, she scores 11/15 (strongly suggestive of depression)
- You prescribe sertaline 25mg daily.
- Four weeks later, you increase it to 50mg daily
- Mr. and Mrs. Zheimer report resolution of symptoms
Mrs. Zheimer

- Mrs. Zheimer is now 89 years old. She is in the moderate stages of Alzheimer’s disease. She is now on 10mg of Aricept

- She is accompanied by her husband. He reports that in addition to her cognitive problems, she has been having occasional emotional outbursts over trivial events, she has called the police reporting that her neighbors are stealing her clothes, and once she ran out of her apartment fearing someone set it on fire.
Mrs. Zheimer

- Mr. Zheimer is pleading with you to help him. He cannot sleep, and cannot leave her alone.

- He tells you he may need to place her in a nursing home if this continues.

- What should you tell him?
Doctor’s dilemma

- You, as her doctor want to help Mr. and Mrs. Zheimer. You consider an ‘off-label’ use of an antipsychotic medication.

- Questions you have:
  - Which one?
  - Will it work?
  - Is it safe?
Dementia and ‘BPSD’

- ‘Behavioral and psychiatric symptoms associated with dementia’
- Definition-the *non-cognitive* psychiatric symptoms
  - Apathy, aggression, agitation, depression, delusions, hallucinations, wandering, repetitive vocalizations
- Prevalence-60-80% of patients with dementia
- Consequences-increase stress, depression in caregivers, nursing home placement, LOS in hospital, cost of care

Lyketsos CG et al. JAMA 2002
Savva GM et al. BJPych 2009
Time line of FDA warnings

- 2002 and 2004 - risperidone and olanzapine may increase risk of cerebrovascular events
- 2003 - ALL atypical antipsychotics may increase blood glucose and risk of diabetes mellitus
- 2005 - ALL atypical antipsychotics increase mortality
- 2008 - conventional antipsychotics were added to this warning
2005 FDA warning

- Atypical antipsychotics may cause a 1.6-1.7 increase in death. The causes of death were varied, but mostly due to cardiovascular (sudden death or congestive heart failure) or infections (pneumonia).
  - Mortality -4.5% (drug treated) vs. 2.6% (placebo)

- Unpublished (posters and presentations) data-analysis of 17 placebo-controlled studies of olanzapine, aripazole, risperidone, quetiapine. N=5106

www.fda.gov
Last accessed March 30, 2011
Risk of Death Associated with Atypical Antipsychotic Drug Treatment for Dementia

- Meta-analysis of 15 Randomized PCT (9 were unpublished)
  - Aripiprazole, olanzapine, risperidone, quetiapine
- Overall 3353 patients were randomized to drug, 1757 patients were randomized to placebo
- Dementia ranged from mild to severe
- Trials were 10-12 weeks on average

Schneider LS et al. JAMA 2005
Risk of death with Atypical Antipsychotics – results

- Mortality incidence of 3.5% (treatment group) vs. 2.3% (placebo) per trial
- Overall odds ratio for death was 1.54 in treated vs placebo groups (95% CI, 1.06-2.23)
- Subgroup analysis-no differences in mortality
  - Degree of dementia
  - Among the 4 drugs

Schneider LS et al. JAMA 2005
Is there anything safe?

- So, we then went back to prescribing ‘conventional antipsychotics’
  - Eg. haloperidol, phenothiazines......
Are ‘conventional antipsychotics’ safe?

- Pennsylvania N=22,890
  - Mortality 17.9% vs 14.6%, HR 1.51

- Ontario N=27,259
  - Mortality: conventional > atypical > no drug
  - HR 1.31

- British Columbia, N=37,241
  - Mortality 14.1% vs. 9.6%

Wang PS et al. NEJM 2005
Schneeweiss S et al. CMAJ 2007
2008 FDA warning

- Conventional and atypical antipsychotics are associated with an increased risk of mortality
- Antipsychotics not approved for dementia related psychosis.
  - No approved drugs for this
- Physicians should discuss this risk of increase mortality with patients, families...

Recommendations for BPSD

- American College of Neuropsychopharmacology (ACNP)
- ‘Good clinical care’
- Shared decision making with pt/family
- Identify target symptoms
  - Establish time frame-expectations, evaluation

Jeste DV et al. Neuropsychopharmacology 2007
ACNP

- Rx: Severe forms - persistent, recurring, significant disruption in function
  - psychosis, agitation
- Lowest doses, shortest time period
- Regularly assess response
- Close monitoring - baseline, every 3 months
  - PE-BP, weight, s/e (EPS, tardive dyskinesia)
  - Labs - glucose, lipids (every 6 months)
Recommendations for BPSD

- American Academy of Neurology (AAN)
- Use medications when environmental interventions fail
- Check blood glucose at baseline
- Atypicals are better tolerated than conventional

Doody RS et al. Neurology 2001
Non pharmacological treatment

- Assess patients needs first
  - Medical (pain, hunger, need to urinate, move bowels)
  - Environmental (need to change position, temperature in room, noise, light)
- Caregiver education
- Music, massage, pet, aromatherapy
Pharmacologic treatment

- Discussion with pt/caregiver on risks/benefits
- Identify specific behaviors
- Choose drug that treats this most closely
- Counsel caregiver to use medications to target those behaviors in addition to the behavioral approaches
- Reassess, revise treatment plan
Mr. and Mrs. Zheimer

- You empathize with Mr. Zheimer
- Discuss the risks and benefits of medications available.
- Refer him to www.alz.org for behavioral interventions.
- For Mrs. Zheimer’s psychotic symptoms (paranoid delusions), you prescribe risperidone 0.5mg by mouth nightly. You explain to Mr. Zheimer your follow up plans to assess her response and monitor for any side effects.
- He is grateful for your time and guidance.
RELAXATION CD'S FOR INSOMNIACS

NON-RELAXATION CD'S FOR NARCOLEPTICS

- OCEANS
- WHALE SONG

- SCREAMING BABY
- CAR ALARMS
- PNEUMATIC DRILLS

© Original Artist
Mister Zheimer

Mrs. Zheimer’s behavior is now stable and the family is managing at home. Her husband has started seeing you for primary care and at a routine visit complains of insomnia. He has hypertension and high cholesterol controlled with medication. No CHF, DM, obesity.

- Difficulty falling asleep
- Awakens each morning around 4am
- Increasing stress about not getting “enough” sleep
- Denies depression

What are your next steps?
Sleep Changes with Aging

- **Decreased**
  - total sleep time and efficiency
  - stage 3 and 4 sleep or slow wave sleep (SWS)
  - rapid-eye movement (REM) sleep
  - # of sleep cycles through per night

- **Increased**
  - daytime napping
  - stage 1 and 2 sleep
  - awakenings and arousals

- Sleep onset or latency becomes delayed
- Circadian phase advanced
Sleep Changes with Aging

<table>
<thead>
<tr>
<th>Sleep Stages</th>
<th>Awake</th>
<th>Non Rapid Eye Movement (NREM)</th>
<th>Rapid Eye Movement (REM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of total sleep (Young/elderly)</td>
<td>2-5%/8-15%</td>
<td>40-50%/60-80%</td>
<td>20%/0-5%</td>
</tr>
<tr>
<td>Characteristic wave forms</td>
<td>Theta waves (4-7 Hz)</td>
<td>Sleep spindles (short bursts of activity between 12-14 Hz) and K-complexes</td>
<td>Delta waves (&lt;4 Hz)</td>
</tr>
<tr>
<td>Clinical Significance</td>
<td>Increased duration suggests sleep fragmentation</td>
<td></td>
<td>Formally divided into stage N3 and N4 based on the % amount of delta waves present. Also referred to as slow wave sleep, Restorative phase of sleep</td>
</tr>
</tbody>
</table>

Sleep Changes with Aging

Insomnia

- Subjective report (initiation and/or maintenance despite adequate opportunity)
- Affecting function, causing daytime somnolence or worry
- Varying frequency/length of time depending on criteria (DSM IV, ICSD-2, ICD-10)
Evaluation

- Primary insomnia
- Secondary
  - Sleep related breathing disorders
  - Anxiety/depression
  - Parasomnias
  - Exacerbation of co-morbid conditions

Non-Pharmacologic Treatment
Primary Insomnia

- Non-pharm
  - Sleep hygiene
  - Cognitive
  - Sleep restriction
  - Stimulus control
  - Relaxation therapy
  - Medication review: d/c antagonizing meds

Pharmacologic Treatment
Primary Insomnia

- Side effect potential
- Prescription:
  - FDA approved for the indication of insomnia (benzodiazepines, nonbenzodiazepine BzRAs, and ramelteon)
  - Non FDA approved:
    • Antidepressants
    • Antipsychotics
    • Anticonvulsants

Pharmacologic Treatment
Primary Insomnia

- Over-the-counter medications
  - Typically antihistamines
  - Risk of delirium, urinary retention, interactions with medications

- Supplements
  - Melatonin
  - Insufficient evidence, but commonly used: kava, valerian, skullcap, passionflower

Mrs. Zheimer

- Mrs. Zheimer has been under your care for 9 years. She has been admitted a third time this year for pneumonia:
  - Decreased oral intake, seems to cough with liquids
  - Bed-bound
  - Stage III pressure ulcer from last month’s admission that has not healed
  - Not responding to antibiotic therapy
  - Family decision to focus on her comfort: declines feeding tube and resuscitation if condition worsens
Case cont’d

- Mrs. Zheimer’s family expresses the following concerns about her symptoms:
  - Not eating
  - Short of breath
  - Increasing confusion

- What can you offer to the patient and family?
Common end-of-life symptoms

- Pain
- Constipation (usually related to opioid treatment)
- Dyspnea
- Depression/anxiety
- Anorexia
- Nausea/vomiting
- Fatigue/debility
- Terminal stages: delirium, seizure, myoclonus
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Strong Recommendations

Moderate Evidence

- In patients with serious illness at the end of life, clinicians should:
  - regularly assess patients for pain, dyspnea, and depression.
  - use therapies of proven effectiveness to manage dyspnea, which include opioids in patients with unrelieved dyspnea and oxygen for short-term relief of hypoxemia.

Dyspnea

- *Subjective* feeling of breathlessness
  - Anxiety
  - Hypoxemia
  - Obstructive/restrictive disease

- Not necessarily correlated with respiratory rate or oxygen saturation, but these can be indicative of dyspnea in a cognitively impaired person
Dyspnea

- Oxygen
  - stimulates V2 branch of trigeminal nerve (fan is good, too)

- Opiates
  - Effective often lower than those used to treat pain
  - Can reduce sx without reductions in respiratory rate or O2 sats

- Anxiolytics
  - Anxiety and breathlessness are tightly intertwined
  - Benzodiazepines, reassurance, relaxation, distraction, and massage therapy may decrease anxiety
  - Cautious use of BZD in older adults

- Other treatments based on individual:
  - diuretics, bronchodilators, and corticosteroids

## Excessive Secretions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine eye drops 1%</td>
<td>One to two drops orally or under the tongue; titrate every eight hours</td>
</tr>
<tr>
<td>Glycopyrrolate (Robunil)</td>
<td>1 mg orally or 0.2 mg subcutaneously or intravenously every four to eight hours as needed</td>
</tr>
<tr>
<td>Hyoscyamine (Levsin)</td>
<td>0.125 to 0.5 mg orally, under the tongue, subcutaneously, or intravenously every four hours as needed</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>One to two patches applied topically and changed every 48 to 72 hours</td>
</tr>
</tbody>
</table>

Anorexia/Cachexia

- Limited evidence:
  - Most large trials for patients with cancer or HIV related anorexia.
  - Small trials related to anorexia in dementia or chronic illness
  - Studies showing weight gain, were related to adipose and not lean muscle weight increases.
  - None showed extension of life
  - Mixed results related to quality of life
Anorexia/Cachexia

- Education and management of expectations
  - Symptoms are a manifestation of worsening disease.
  - Encourage favorite foods.
  - Remove food restrictions.
  - Alcohol can be appetite stimulant in select patients

Anorexia/Cachexia

- Pharmacologic:
  - Corticosteroids
    - Dexamethasone is advantageous in that it allows once a day dosing, has minimal mineralocorticoid properties, and may improve mood and energy
  - Megestrol acetate
  - Cannabinoids

- Side effects and risks of therapy may outweigh benefits.

Fatigue

- Prevalence 8-53%
- Poorly understood and little evidence for effective treatments
- Treat reversible underlying conditions
- Energy conservation in advanced disease
- Incremental exercise for those functional but sedentary
- No proven medication interventions
Terminal Delirium

- Experienced in up to 85% in last weeks of life
- Identify underlying/reversible causes.
- Ensure an appropriately calm environment with caregivers/family at bedside.

Delirium: Non-pharmacotherapy

- Minimize the use of immobilizing catheters, intravenous lines, and physical restraints
- Provide visual and hearing aids
- Control pain
- Monitor bowel and bladder functioning

- Review medications
- Reorient communications with the patient
- Facilitate sleep hygiene measures, including relaxation music or tapes at bedtime, warm drinks, and gentle massage

Delirium: Pharmacotherapy

- Limited evidence of efficacy
- Neuroleptics
  - Haloperidol (0.5mg every 4 hours as needed, titrated to symptoms) or an atypical antipsychotic.
  - Chlorpromazine may be used as alternative
- Benzodiazepines should be avoided as they have been shown to worsen delirium.

Mrs. Zheimer

- Morphine 2mg IV every 4 hours for management of dyspnea.
- O₂ via nasal canula
- Scopolamine patch for reducing secretions and d/c IV fluids
- Haloperidol 0.5mg every 4 hours prn agitation/confusion
- Arrangements for home hospice
Mrs. Zheimer

- Discharged home with hospice
- Morphine liquid used 2mg every 4 hours as needed for dypsnea
- Expired with family at bedside 2 weeks later.
- Family calls to express appreciation of your care and support of the year.
- Mister Zheimer has a follow up appointment in 2 weeks.