Best Practices in Dementia Care: Do's and Don'ts

Webinar February 11, 2016 at 1:00PM

Speakers:

Jay S. Luxenberg, M.D

&

Janice Hoffman, PharmD, CGP, FASCP

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Timothy Gieseke, MD	Planner	None	
Janice Hoffman, Pharm.D, CGP, FASCP	Faculty / Planner	Grant Recipient, PI Research	Novartis
Barbara Hulz	Planner	None	
Jay Luxenberg, MD	Faculty	None	
Renee McNally	Planner	None	
Dan Osterweil, MD, FACP, CMD	Planner	None	
Michael Wasserman, MD	Planner	Honoraria, Editorial Board for Merck Manual	Merck

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Dementia in the Nursing Home

Jay S. Luxenberg, M.D.
Chief Medical Officer, On Lok
Clinical Professor,
University of California, San Francisco

Learning Objectives

By participating in this webinar participants will have the ability to:

- Understand the value of making a diagnosis of etiology for management of dementia
- Recognize how describing a troublesome behavior is one of the first steps in managing it
- Describe the “ABC”s of behavior management
- Perform a Risk of Harm assessment to be able to correctly determine the risk/benefit ratio of proposed interventions

What's the Big Deal?

- Dementia is more costly than any other disease, even cancer and heart disease
- The biggest driver of costs is residential care
- The biggest trigger for inability of family to provide care and need for residential care is behavioral symptoms

What's the Big Deal?

- The personal toll of behavioral symptoms on family and paid caregivers is huge, with emotional strain and physical injury
- Our ability to eliminate behavioral symptoms of dementia with pharmacotherapy is very, very limited due to weak efficacy and prominent side-effects.

Importance of Etiology

- Dementia is a syndrome, not a disease.
- The cause (etiology) of a dementia has important implications for prognosis, treatment and clinical presentation of behavioral symptoms

Importance of Etiology Examples

- Dementia with Lewy Bodies (DLB) often causes recurrent visual hallucinations that are typically well formed and detailed
- DLB patients often have rapid eye movement (REM) sleep behavior disorder where they act out vivid, often unpleasant dreams with vocal sounds and sudden, often violent arm and leg movements during REM sleep

Importance of Etiology Examples

- Dementia with Lewy Bodies (DLB) patients generally have severe neuroleptic sensitivity limiting the use of antipsychotic drugs due to unacceptable side-effects

Importance of Etiology Examples

- Behavioral Variant Frontotemporal dementia patients present differently than Alzheimer patients – they are usually younger, they have prominent early psychiatric symptoms including apathy, disinhibition, and unusual eating patterns
- Almost zero evidence base for drug treatment of behavioral symptoms, but serotonergic deficit means SSRIs often 1st line. EPS limits use of antipsychotics

Importance of Etiology Examples

- Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17) patients often have delusions, hallucinations, and slowness of movement and tremor as seen in Parkinson's disease.
- Typical behavioral/personality characteristics include apathy, defective judgment, and compulsive and abusive behavior.
- Poorly tolerated extrapyramidal side effects with the use of antipsychotic drugs similar to other forms of FTD

Bottom line: having a diagnosis for the dementia syndrome is important

Billion Dollar Question

- Why do some persons with dementia exhibit prominent behavioral or psychological symptoms of dementia (BPSD) and others do not?

A Poll

- In your opinion, what is the predominant factor precipitating agitated behavior in dementia?

1. Attempted personal care, e.g. dressing or showering
2. Biological predisposition interacting with the dementing illness
3. Delirium
4. Frightening hallucinations or delusions

Biology of BPSD

- Increasing evidence that there is a genetic interaction between the dementia and the predisposition for behavioral symptoms
- Specific candidate genes for specific symptoms like hallucinations
- At this point, not yet clinically useful (but certainly interesting!)

Biology of BPSD

- Disease-dementia interactions are common – e.g. vision and hearing deficits associated with more BPSD symptoms; arthritic and other painful conditions can manifest as behavioral symptoms, vascular dementia has more depression, etc.

Biology of BPSD

- Certain diseases predispose to delirium, which can manifest as behavioral symptom – e.g. Paget's disease or hyperparathyroidism where dehydration or bedrest can trigger hypercalcemia which can cause delirium.

What's First?

- For a new behavioral problem, an initial medical evaluation will look for delirium, including intercurrent illness.
- Presence of infection, fecal impaction, inadequately treated pain, hypoxia, dehydration, electrolyte abnormality, etc. need to be assessed and addressed while the behavior itself is being analyzed and care strategy formulated.

Managing Difficult Behaviors

- Characterize the behavior that is causing a problem
  - Whose problem? Is it causing distress to the patient or the caregivers or other people?
  - Is it resistance to personal care, verbal aggression, sleep cycle disruption, etc.?
  - What are the antecedents (triggering factors), circumstances (time, location, specifics of interpersonal factors, etc.)

Managing Difficult Behaviors

- Is the behavior simply due to the memory impairment?
  - Common issue for caregivers is the patient who needs assistance for safe transfer, who can't remember that or who lacks insight into their deficits, so they attempt self transfer and fall over and over again

Managing Difficult Behaviors

- What were the consequences of the problematic behavior?
  - Did the family or professional caregiver respond with angry words, redirection, a physical response, etc.
  - Was there an effect on the environment: e.g. other dementia patients yelling or getting physically violent with the patient?

ABC of Behavior Management

- This strategy, of identifying the antecedent, characterizing the behavior, and analyzing the consequences leads to a mnemonic:
  - Activating event
  - Behavior
  - Consequence
- This information is a necessary part of developing a treatment strategy

Activating Event Analysis

- It helps to put yourself in the patient's place – imagine being demented and then interpret their experience
- To what degree was fear or anxiety a contributing factor? This can influence how you manage behavior.

Unmet Needs Analysis

- Environmental discomfort – wet, hot, etc.
- Internal discomfort – nausea, dizziness, abdominal bloating, shortness of breath, etc.
- Pain
- Boredom
- Frustration (e.g. with expressive aphasia)
- Fear (e.g. misinterpretation of noises, care actions, shower, etc.)

Unmet Needs Analysis

- Loneliness
- Lack of privacy
- Lack of peace and quiet
- Invaded personal space
- Lack of exercise
- Lack of respect for cultural factors
- Inability to communicate

High Yield Assessments

- Impaired vision – check glasses use
- Impaired hearing – check hearing aids, wax
- Thirst or hunger
- Pain
- Constipation or fecal impaction
- Urinary retention
- Sleep disturbances – including rhythm
- Change in usual routine – including caregivers, family, roommate, environment

Risk of Harm Assessment

- To self – falls, elopement, malnutrition, suicide
- From others – physical response to intrusive behaviors, caregiver abuse
- To others – physical aggression, sexual disinhibition
- Miscellaneous – loss of home, social isolation, caregiver stress, need for distant placement

Reassessment

- Once a treatment/care plan is developed, frequently reassess for efficacy, and for changes in biopsychosocial factors.
- Understand that behaviors in dementia do fluctuate, and utilize patience before adapting care strategy.

Nonpharmacological Therapy

- Person-centered care
- Caregiver and family education
- Identify residual strengths and abilities
- Modify communication, environment, meaningful activities
- Consider specific therapies:
  - Behavior management
  - Aromatherapy
  - Music
  - Validation Therapy
  - Reminiscence Therapy
- Do not stop trying new elements of non-pharm care – it is an iterative process!

Nonpharmacological Therapy

- Absolutely great resource: A Systematic Evidence Review of Non-pharmacological Interventions for Behavioral Symptoms of Dementia (BPSD) (VA's Health Services Research & Development Services HSR&D's) Evidence-based Synthesis Program (2011)

  http://www.hsrd.research.va.gov/publications/esp/Dementia-Nonpharm.pdf

- Summary – evidence based medicine documentation is disappointing, but consensus is that non-pharm approaches still worth starting with and continuing to refine with experience with individual patient's responses

Open Source Reviews

- Livingston, G., Kelly, L., Lewis-Holmes, E., Baio, G., Morris, S., Patel, N., et al. (2014). A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia. Health Technology Assessment (Winchester, England), 18(39), 1–226– v–vi.
- Gitlin, L. N., Kales, H. C., & Lyketsos, C. G. (2012). Nonpharmacologic management of behavioral symptoms in dementia. JAMA: Journal of the American Medical Association, 308(19), 2020–2029.

Poll

- In your opinion, if pharmacotherapy for agitation is indicated, what would your first line choice be?

1. Antipsychotic
2. Benzodiazepine
3. SSRI (antidepressant)
4. Anticonvulsant
5. Apple Juice
6. Other

Pharmacotherapy: Where are we?

- Many families of medications have been proposed for managing agitated behaviors in dementia
- Most that have been studied adequately fail to differentiate from placebo
- The best data for efficacy remains that reported for the antipsychotics – NNT≈7
- Unfortunately, the side effects of antipsychotics include death and cognitive impairment
- The data supporting other medications – antidepressants, cholinesterase inhibitors, valproate, etc. is much weaker or non-existent

Cognitive effects of Atypical Antipsychotics

- In CATIE-AD, atypical antipsychotics were associated with worsening cognitive function at a magnitude consistent with 1 years deterioration compared with placebo.
- For comparison, RCT data show only a 3-6 month's worth cognitive function improvement with cholinesterase inhibitors
- Drugs in CATIE-AD were olanzapine, quetiapine, and risperidone

Vigen CLP, Mack WJ, Keefe RSE, Sano M, Sultzer L, Stroup TS, et al. Cognitive effects of atypical antipsychotic medications in patients with Alzheimer's disease: outcomes from CATIE-AD. Am J Psychiatry. 2011 Aug;168(8):831–9.

Excess Mortality with Atypical Antipsychotics

- Odds ratio of death in randomized, placebo-controlled trials (≈ 3300 patients) was 1.54
- Number-needed-to-harm = 100 (95% CI 53-1000)
- NNT ranged from 4-12 – therefore for every 9-25 people helped there was one excess death

Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. JAMA. 2005;294(15):1934-1943.

- If anything, risk with typical antipsychotics is worse

Musicco M, Palmer K, Russo A, Caltagirone C, Adorni F, Pettenati C, et al. Association between Prescription of Conventional or Atypical Antipsychotic Drugs and Mortality in Older Persons with Alzheimer's Disease. Dement Geriatr Cogn Disord. 2011;31(3):218-224.

Antipsychotics

- Excellent up-to-date review:
  - Ballard C, Creese B, Corbett A, Aarsland D. Atypical antipsychotics for the treatment of behavioral and psychological symptoms in dementia, with a particular focus on longer term outcomes and mortality. Expert Opin Drug Saf. 2011 Jan. 1;10(1):35-43.
- Need to balance modest efficacy versus 1.5-1.8x mortality rate in 12 week studies – longer term excess mortality less well defined but likely present
- In general, best practices would be to use antipsychotics much less often than in past

What Next?

- Remember that the placebo effect in clinical trials is very high – very few active treatments have been shown to exceed it.
- Always implement multiple non-pharmacologic therapies, and continue to add/change them as drug therapy is added if necessary.
- Consider lowest toxicity treatment if treatment is indicated but not urgent:
  - Aromatherapy?
  - Second line would be drugs with more side-effects like SSRIs

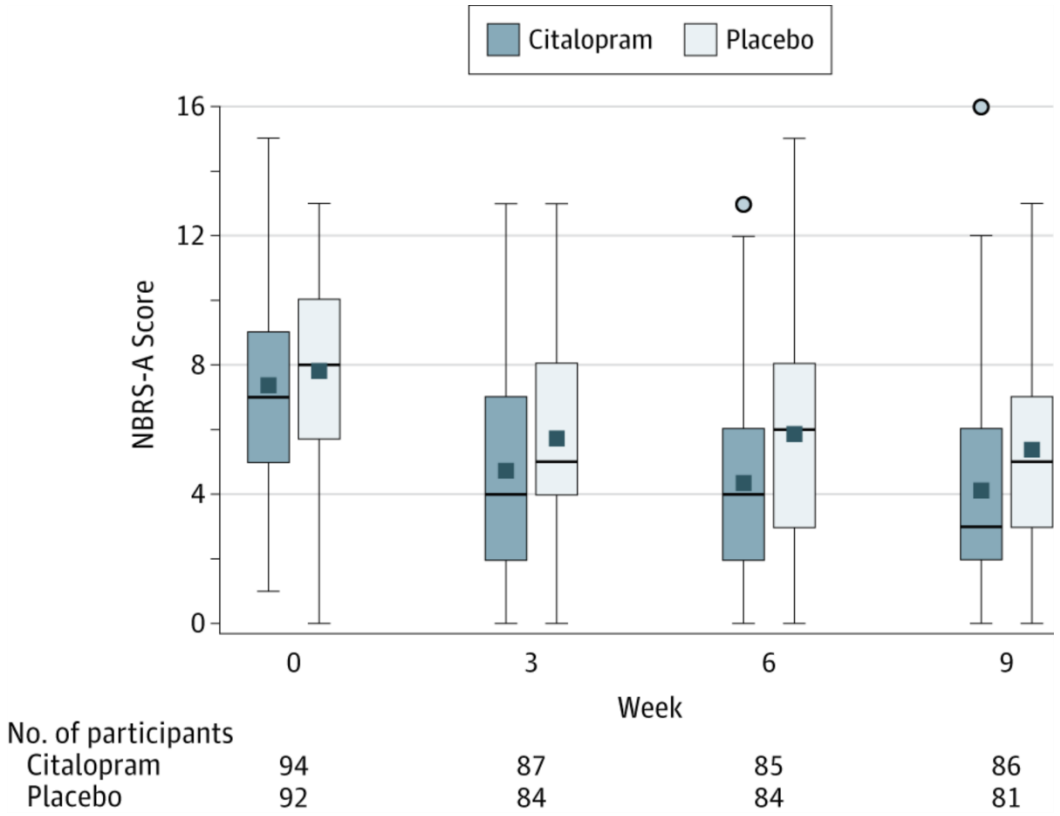
Antidepressants for Agitation in AD

- Three studies have found some benefit of citalopram or sertraline for treating NPS of dementia when compared to placebo.
- Recent JAMA report showing citalopram (10-30 mg) improved agitation compared to placebo when added to non-pharm strategies, with small decrement in cognition detected.

Seitz DP, Adunuri N, Gill SS, Gruneir A, Herrmann N, Rochon P. Antidepressants for agitation and psychosis in dementia. Cochrane Database Syst Rev. 2011;2:CD008191.

Porsteinsson AP, Drye LT, Pollock BG, Devanand DP, Frangakis C, Ismail Z, et al. Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial. JAMA. 2014 Feb 19;311(7):682–91.

From: Effect of Citalopram on Agitation in Alzheimer Disease: The CitAD Randomized Clinical Trial



JAMA. 2014;311(7):682-691.
doi:10.1001/jama.2014.93

Figure Legend:
Neurobehavioral Rating Scale (NBRS)-Agitation Subscale - Higher NBRS scores indicate more severe symptoms. The horizontal bar inside the boxes indicates the median, the square in the boxes indicates the mean, and the lower and upper ends of the boxes are the first and third quartiles. The whiskers indicate values within 1.5 × the interquartile range from the upper or lower quartile (or the minimum and maximum if within 1.5 × the interquartile range of the quartiles) and data more extreme than the whiskers are plotted individually as outliers.

From: Effect of Citalopram on Agitation in Alzheimer Disease: The CitAD Randomized Clinical Trial

- Study design - Dosage began at 10 mg per day with planned titration to 30 mg per day over 3 weeks based on response and tolerability.
- At week 9, 78% of the sample were receiving 30 mg citalopram daily and 15% were receiving 20 mg citalopram daily.
- Citalopram was associated with significant cognitive decline, and greater increase in QTc interval than placebo, and more participants in the citalopram group showed a QTc increase of greater than 30 ms from enrollment to week 3 than participants in the placebo group (7 vs 1; Fisher exact P = .05). Four participants (3 citalopram and 1 placebo) showed QTc prolongation (>450 ms for men and >475 ms for women).
- On August 22, 2011, the US Food and Drug Administration (FDA) issued an advisory regarding dose-dependent risk of QT prolongation with citalopram therapy. The FDA now recommends that elderly patients take no more than 20 mg citalopram daily for any indication.

The CitAD Quandary

- Efficacy of citalopram predominantly demonstrated at a dose of 30 mg. We just don't know if 20 mg would show significant efficacy in a similar design
- Escitalopram is the enantiomer with antidepressant efficacy and it shows less QT prolongation than citalopram and therefore has no similar FDA advisory, but we also have zero evidence of its efficacy for behavioral disturbance in dementia

- Sad conclusion - we need more data!

Valproate

- No evidence of efficacy
- Black box warnings for fatal hepatotoxicity, pancreatitis and teratogenicity

Lonergan E, Luxenberg J. Valproate preparations for agitation in dementia. Cochrane Database Syst Rev. 2009;(3):CD003945.

Benzodiazepines

- No evidence of efficacy
- Fall risk
- Worsening of cognitive impairment
- Withdrawal phenomenon
- Should be used rarely if at all
- “Benzodiazepines are good for delirium” ☺

Short-acting Benzodiazepines versus other Strategies for the Management of Agitation in Older Patients: Clinical Effectiveness and Guidelines. Source: Canadian Agency for Drugs and Technologies in Health (CADTH) Health Technology Assessment published 6/28/2010

Cholinesterase Inhibitors

- The CALM-AD study compared donepezil with placebo in moderate to severe AD subjects with clinically significant agitation that had not responded to a 4-week non-pharmacological intervention, so mirroring usual clinical practice.
- There was no significant benefit of donepezil over placebo in reducing agitation.

Howard RJ et al. Donepezil for the treatment of agitation in Alzheimer's disease. N Engl J Med. 2007 Oct. 4;357(14):1382–1392.

Cholinesterase Inhibitors / Memantine

- The effect of adding memantine to cholinesterase inhibitors is not clear. An initial study showed clear benefit in cognitive and non-cognitive symptoms (again agitation and irritability responding best) when memantine was added to donepezil therapy (Tariot et al., 2004).
- However, more recent RCTs have been negative (Fox et al, PLoS ONE. 2012;7(5):e35185).

Everybody Must Not Get Stoned

- Medical marijuana and tetrahydrocannabinol have been studied in small studies and so far have NOT shown efficacy

van den Elsen, G. A. H., Ahmed, A. I. A., Verkes, R.-J., Feuth, T., van der Marck, M. A., & Olde Rikkert, M. G. M. (2015). Tetrahydrocannabinol in Behavioral Disturbances in Dementia: A Crossover Randomized Controlled Trial. *The American Journal of Geriatric Psychiatry*, *23*(12), 1214-1224

Placebo

- Placebo response in clinical trials for BPSD is really high – this is consistent, and should make us even more willing to pursue non-pharmacologic strategies

Rosenberg, P. B., Drye, L. T., Porsteinsson, A. P., Pollock, B. G., Devanand, D. P., Frangakis, C., et al. (2015). Change in agitation in Alzheimer's disease in the placebo arm of a nine-week controlled trial. *International Psychogeriatrics*, *27*(12), 2059–2067.

Big Guns - ECT

- Small studies have shown safety and efficacy for electroconvulsive therapy for agitation and aggression in patients with dementia whose behaviors are refractory to medication management

Safety and utility of acute electroconvulsive therapy for agitation and aggression in dementia. (2015). Safety and utility of acute electroconvulsive therapy for agitation and aggression in dementia., *30*(3), 265–273.

Apathy

- Some evidence non-pharm treatment is efficacious out of 56 studies, but no consensus on best approach.

  Brodaty H, Burns K. Nonpharmacological Management of Apathy in Dementia: A Systematic Review. Am J Geriatr Psychiatry. 2012 *20*(7), 549–564

- Cross-over RCT – music, art therapy and psychomotor activity better than nothing (duh) .

  Ferrero-Arias J et al. The efficacy of nonpharmacological treatment for dementia-related apathy. Alzheimer Dis Assoc Disord. 2011 Jun.;25(3):213–219.

- Very limited evidence of efficacy for methylphenidate.

  Dolder CR, Davis LN, McKinsey J. Use of psychostimulants in patients with dementia. Ann Pharmacother. 2010 Oct.;44(10):1624–1632.

Apathy

- Apathy in Dementia Methylphenidate Trial 2 (ADMET 2) is a Phase III, placebo-controlled, masked, 6 month, randomized clinical trial sponsored by National Institutes of Aging involving 200 participants with Alzheimer's disease (AD). It has not yet opened for enrollment as of 2015
- ADMET 2 is designed to examine the efficacy and safety of methylphenidate as treatment for clinically significant apathy in AD participants.
- ADMET 2 will enroll participants from real world settings such as outpatient, nursing home, and assisted living facilities and will examine the effects of methylphenidate on apathy and cognition.

clinicaltrials.gov/ct2/show/NCT02346201

Recent Open Access Review

- Panza, F., Solfrizzi, V., Seripa, D., Imbimbo, B. P., Santamato, A., Lozupone, M., et al. (2015). Progresses in treating agitation: a major clinical challenge in Alzheimer's disease. *Expert Opin Pharmacother*, *16*(17), 2581–2588.

Final Thoughts

- Step back and analyze where “push” for pharmacotherapy is coming from – is it because of resistance to care, for vocalizations distressing to others or physical aggression that is dangerous to others, or is there strong evidence that the patient is experiencing distress.
- Redouble efforts to manage environment and interactions with patient to handle behaviors without medications if possible
- If ever documentation of your thought process was important, the use of medications for behavioral management in dementia is it.

Final Thoughts

- If antipsychotics are considered, ask yourself and then the responsible party – “Is a 1 out of 7 chance that I will improve these symptoms (compared to placebo use) worth a 1/100 chance I will cause a death over the next 12 weeks?”
- If the answer is “yes”, document this discussion. I suggest documenting a dose range that is not associated with excess morbidity e.g no more than 2 mg risperidone. That way if higher dose is needed, you will be forced to document discussion of the higher risks of sedation and other side-effects.

Final Thoughts

- Given the shift in the acceptable risk-benefit equation for antipsychotics, a reasonable goal could be to monitor your personal percentage of antipsychotic prescription or the use in your facility or practice in dementia patients

Best Practices in Dementia Care: Antipsychotic Use

Janice Hoffman, PharmD, CGP, FASCP

Learning Objectives

By participating in this webinar participants will have the ability to:

- Overview of the role for Antipsychotics in Dementia
- Explain a best practice for transferring a patient from the acute hospital to a SNF with an antipsychotic order
- Describe best practice for behavior monitoring with antipsychotic medications
- Monitor effect and side effects of antipsychotic drugs
- Identify alternative non-antipsychotic medications

Antipsychotic Use in Dementia

- Evidence shows risks are greater than benefits for using Antipsychotics for many patients
- Non-drug interventions first
  - control your own voice and responses: **stay calm, tolerate behavior, redirect**
- Use Alzheimer's disease meds first
  - acetylcholinerase inhibitors (Donepezil, Rivastigmine, Galantamine)
  - NMDA antagonist (Memantine)
- Use only for psychosis associated with Dementia for limited duration (≤12 wks)
  - Document treatment targets BEFORE any intervention
  - Monitor outcomes and adjust approach
  - Is the medication meeting targets? Improving quality of life?

HHS – OIG 2011 report on Antipsychotics

- 304,982/2.1 million 14% of at least 1 Medicare claim for an atypical antipsychotic (1/07 to 6/07)
  - Estimated cost $309 million
- 83% of Atypical Antipsychotics were used for off-label indications
  - 88% for indications in the FDA black box warning (not supposed to be prescribed)
- Over 700,000 of the 1.4 million atypical antipsychotics were “erroneous” costing $116 million
  - Not documented as being administered
  - Not used for a medically accepted indication
- 22% were not administered in accordance with CMS guidelines of unnecessary drugs ($63 million)

Transition Case

- Mary, age 87, female, who is being transferred from the acute hospital s/p a fall sustained hip fracture after an ORIF. She was living in an ALF prior to hospitalization
- Her medication reconciliation

BEFORE HOSPITAL	ON TRANSFER BACK TO SNF
Ramipril 10mg daily	Lisinopril 20mg daily
Amlodipine 5mg daily	Furosemide 20mg daily
Tums PRN GI upset	Pantoprazole 40mg daily
Centrum Silver daily	MVI w/min daily
Levothyroxine 25mcg daily	Risperidone 0.5mg qHS for screaming
Sertraline 25mg qAM	Citalopram 10mg qAM
Donepezil 5mg qAM	Lorazepam 0.5mg q4h PRN anxiety
Memantine 10mg BID	Zolopidem 5mg qHS PRN sleep
Acetaminophen 500mg TID	Norco 5/325mg q4h PRN pain
Ibuprofen 200mg PRN pain	Hydromorphone 1mg IV q2h PRN severe pain

What should happen with Mary's Care?

- Lab tests
  - Thyroid tests (Levothyroxine)
  - Renal panel (Furosemide)
- Nursing interventions and behavioral care plan
  - Screaming – observe without risperidone
  - Consult geriatrician/psychiatrist
- Add medications
  - Add back Levothyroxine and adjust per labs
  - Add back Donepezil and Memantine
  - Consider calcium w/ Vitamin D
  - Acetaminophen?
- Discontinue medications
  - Hydromorphone
  - Lorazepam
  - Risperidone?

Question #1

- Which of Mary's psychiatric medications on the reconciliation may not be needed?

A. Risperidone

B. Citalopram

C. Zolopidem

D. A and C

E. A, B and C

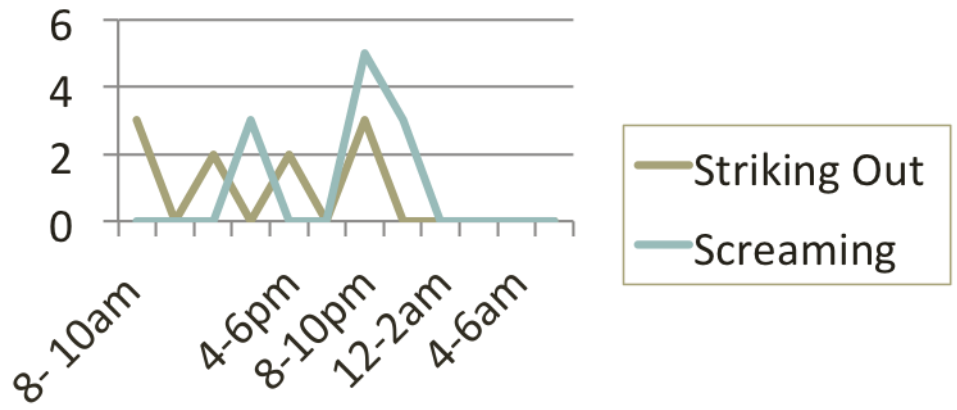
Defining Behavior Targets for Antipsychotic Use

- Hallucinations IF distressing
- Delusions
  - stealing things can be a memory related issue
- Aggressive behavior
  - if is a danger to resident or others
- Persistent, distressing behaviors that are a danger to the resident (usually don't respond well to Antipsychotics)
  - Significant decline in function (ex. screaming)
  - Unable to receive needed care (ex. bathing battles)

Behavior Mapping

- Short observation period: 15min intervals
- Over 1-4 days
- Tracking behaviors for:
  - Frequency
  - Intensity
  - Duration
  - Time of day

- Consultant pharmacist can assist by looking at behavior patterns and make recommendations as to:
  - Timing of medication
  - Nature of prescription

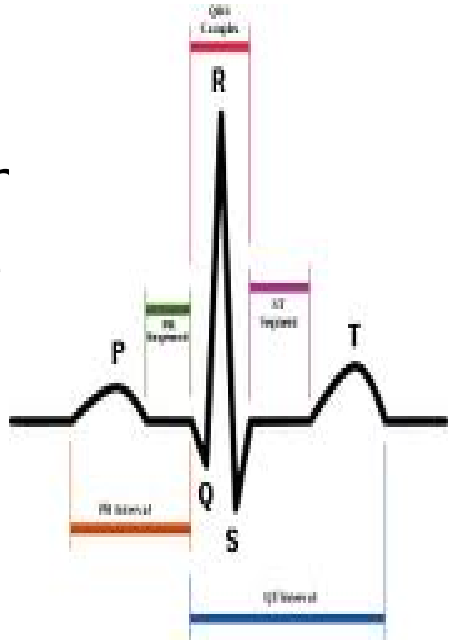


Regulations for Behavioral Medications

- Federal – FTag – 329 – unnecessary medications due to:
  - Duration
  - Excessive dose or duplicate
  - Insufficient monitoring
- Federal FTag 329 Gradual Dose reductions GDR
  - *Guidelines Dementia Alzheimer's type with behaviors*
    - *Antipsychotic Use – 1st year 2 quarters attempt reductions*
    - *Other psychotherapeutic agents- during 1st year 2 quarters attempt reductions*

Risks of Antipsychotic Use in the Elderly

- Antipsychotics are not indicated for the treatment of dementia-related psychosis.
- Black Box warning for use in dementia – 1.6 to 1.7 fold increase risk of death (sudden cardiac, stroke, pneumonia)
- Sensitivity to Adverse Effects
  - EKG changes: QTc interval prolongatior
  - Movement disorder (EPS) – irreversible
  - Low BP upon rising – risk of a fall
  - Diabetes
  - Hyperlipidemia
- Family dynamics - risk of legal action(?)



Withdrawal of an Antipsychotic in Patients with Dementia

- If there is NO Benefit within 1 month STOP the medication
- Taper should be slow over days/weeks/months (depending on individual response to taper)
  - The longer taking the medication slower/faster it can be withdrawn- individualize
- Risperidone use effective for 4-6 months may see risk of relapse (NEJM Oct 2012 367;16: 1497-507)
- Withdrawal behaviors (during taper or after stop x 6 wks)
  - Anxiety and irritability
  - Verbal or physical outbursts

Question #2

Which of the following side effects may contribute to an increased risk for mortality associated Atypical Antipsychotic use in the elderly (especially if they have DNR in their POLST)?

A. Diabetes
B. Hyperlipidemia
C. Movement disorders
D. QT prolongation

Highest Risk Antipsychotics Agents for Hypotension

- Risperidone:
  - Tachycardia (1% to 5%)
  - Hypertension (I.M. injection 3%)
  - Postural hypotension (≤2%)
  - Hypotension (≤1%)

- Olanzapine: (1% to 10% for each)
  - Chest pain, tachycardia
  - Hypertension, postural hypotension
  - Peripheral edema

- Clozapine:
  - Black Box Warning: Orthostatic hypotension
  - High affinity for the alpha 1 receptor
  - Seen in 25% of geriatric patients

Case #2

MJ is a male age 79 who has lost 20 lbs in the past 6 months and currently weighs 125 lbs at 5’ 9” tall. He is refusing meals and is having occasional bouts of loose stool/diarrhea. His meds are as follows :

- Donepezil 10mg qHS (Alzheimers)
- Memantine 10mg BID (Alzheimers)
- Metoprolol XL 50mg po daily (HTN)
- MVIw/ min 1 tab po daily (supplement)
- Fish Oil (omega 3) 1gm BID (cholesterol)
- ASA 81mg po daily (CVA prevention)
- Tamsulosin 0.4mg qHS
- Megestrol 40mg po daily (weight loss)
- Vitamin B-12 1000mg IM monthly (supplement)
- Fluoxetine 40mg po qAM (depression)
- Olanzapine 5mg ODT at 12Noon + 5mg PRN (pacing the halls; refusing meals)
- Valproic acid 250mg po q5pm (sundowning)

Medication Regimen Raising ADR of concerns

Weight loss

- Donepezil
- Prozac
- Megestrol at low doses

Weight gain

- Zyprexa
- Depakote

Cardiac

- Zyprexa (lower)
- Prozac
- Donepezil

Lower BP

- Zyprexa
- Donepezil
- Tamsulosin

Question #3

Sally, age 75, is a patient who presents with a complaint of always being tired and the MD wants to use a antipsychotic to treat Sally's hallucinations that Staff is stealing her food--which of the following Atypical Antipsychotics would be the best choice (with the least sedation)?

A. Clozapine (Clozaril)
B. Olanzapine (Zyprexa)
C. Aripiprazole (Abilify)
D. Quetiapine (Seroquel)

Weight Gain

- Weight gain observed with atypical antipsychotic agents is usually accompanied by metabolic abnormalities like:[16]
  - Dyslipidemia-Weight gain and dyslipidemia are concordant of each other[16]
  - Diabetes risk
- Diabetes risk maybe independent of weight gain[16]
- Weight gain and metabolic abnormalities are linked to increased risk of cardiovascular disease[16]

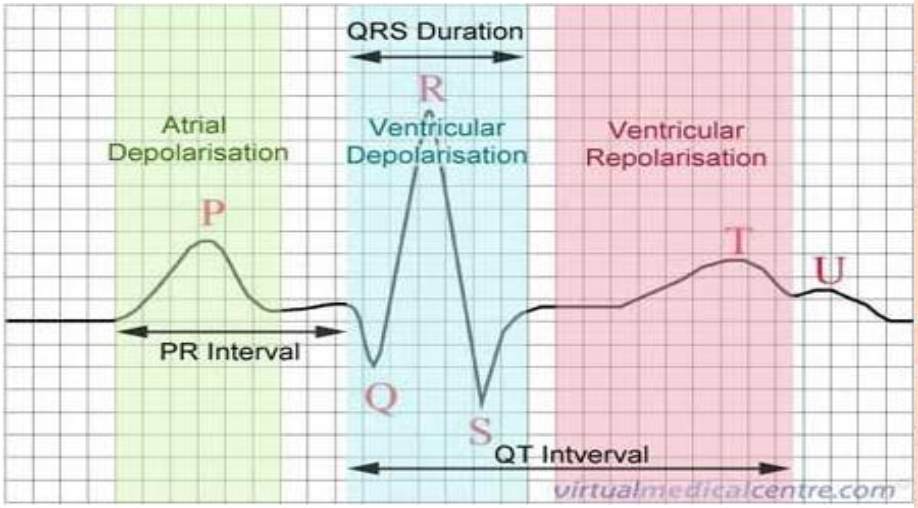
Question #4

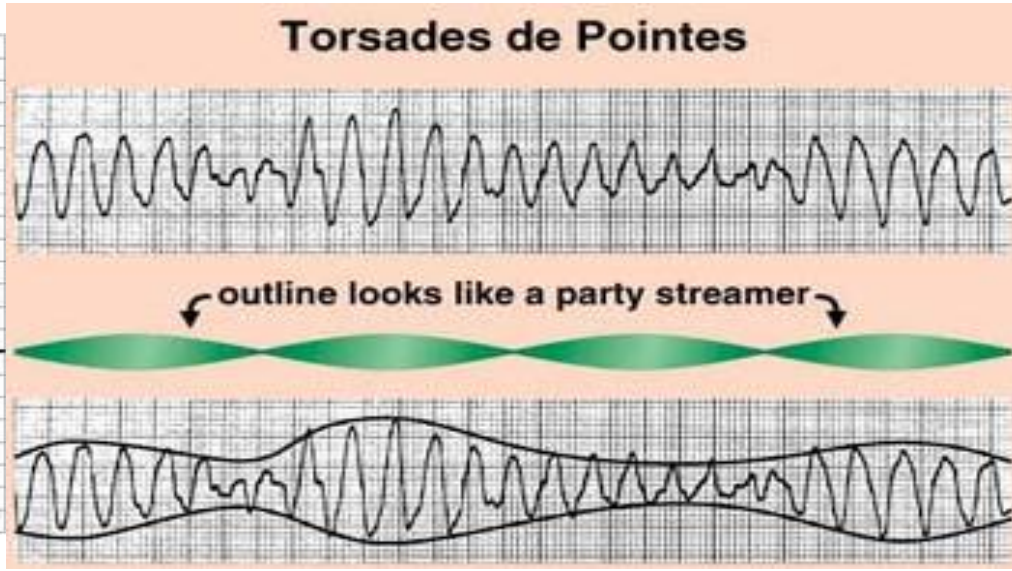
Jared, age 87, is a male patient who is 6’ 3” tall and weighs 310lbs. In addition, he has Diabetes Type II and high cholesterol and Bipolar Disorder. Since he has been hallucinating and it is causing him distress, the PCP wants to add an antipsychotic to his mood stabilizer of Valproic acid. Which antipsychotics might be a possible good choice?

A. Clozapine (Clozaril) or Olanzapine (Zyprexa)
B. Olanzapine (Zyprexa) or Risperidone (Risperdal)
C. Risperidone (Risperdal) or Quetiapine (Seroquel)
D. Aripiprazole (Abilify) or Paliperidone (Invega)

QTc Prolongation

- QT interval: represents both the depolarization and repolarization of the ventricles on a ECG[21]
- QTc interval: QT interval shortens with increasing heart rate and QTc corrects for it[21]
- A QTc interval of <440 msec → normal
- A QTc interval of >500 msec→ clinically used as cutoff point → greater risk of Torsade de Pointes.





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QTc Prolongation: Torsade de Pointes

Factors that increase risk of TdP and/or sudden death in association with drugs contributing to QT prolongation:

(1) bradycardia

(2) hypokalemia or hypomagnesemia

(3) concomitant use of other drugs that prolong the QTc interval (ie. Beta blockers, AChE-I, Digoxin)

SGA Cardiovascular Side Effect Summary [19]

Drug[1]	OH	WT GAIN	Lipid	DM	QTc
ARIPiprazole (Abilify®)	Low	Very low	Very low	Very low	Low
Asenapine (Saphris®)	Low / moderate	Low	Very low	Very low	Low
CloZAPine (Clozaril®)	High	High	High	High	Low
Iloperidone (Fanapt™)	Low / moderate	Low / moderate	Very low	Very low	Moderate
Lurasidone (Latuda®)	Low	Very low	Very low	Very low	Low
OLANZapine (ZyPREXA®,ZyPREXA® Zydis®)	Low / moderate	High	High	High	Low
Paliperidone (Invega™)	Moderate	Low	Low	Low	Low
QUEtiapine (SEROquel®)	Moderate	Moderate	Moderate	Low / moderate	Low
RisperiDONE (RisperDAL®)	Moderate	Low / moderate	Low	Low / moderate	Low
Ziprasidone (Geodon®)	Low	Very low	Very low	Very low	Moderate[4]

OH: Orthostatic Hypotension; DM: Diabetes Mellitus;
QTc: correct QT interval prolongation

ADR: Orthostatic Hypotension and Tachycardia

- **High Risk**: Clozaril[19]
- **Moderate**: Seroquel, Risperdal, Invega[19]
- **Low/Moderate**: Saphris, Fanapt, Zyprexa[19]
- **Low**: Abilify, Latuda, Geodon[19]
- Bottom Line:
  - Avoid Clozaril, Seroquel, Risperdal, and Invega
  - Try Abilify, Latuda, or Geodon

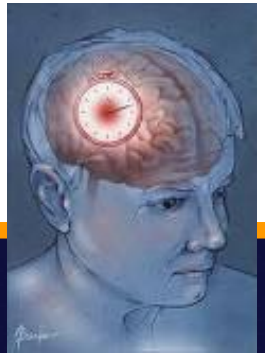
Question #5

Fred has a history of bradycardia. Since the MD wants to start an Antipsychotic to treat his behaviors which ones may be the best choice given his risk for QT prolongation?

A. Lurasidone (Latuda) or Olazapine (Zyprexa)
B. Ziprasidone (Geodon) or Risperidone (Risperdal)
C. Risperidone (Risperdal) or Paliperidone (Invega)
D. Clozapine (Clozaril) or Iloperidone (Fanapt)

Stroke

- Clinical placebo controlled trials of Zyprexa, Risperdal, and Abilify demonstrated elevated incidence of stroke among elderly patients with dementia[24]
  - Observational studies found no difference in incidence of stroke between Zyprexa, Risperdal, Abilify, Geodon and Seroquel [34]
  - Observational studies show both increase risk and no increased risk with SGA use[34]
- Bottom line:
  - No clear evidence of whether SGA increase risk of stroke in elderly patients with dementia[34]



Alternative prescription medications to the Antipsychotic Agents

- If low cardiovascular risk
  - Citalopram
- For mood stabilization/aggression
  - Anticonvulsants
    - Valproic acid
    - Lamotrigine
    - Oxcarbazepine
  - Propranolol
- Behaviors with potential neuropathic chronic pain issues
  - Duloxetine
  - Venlafaxine
  - Gabapentin

Vitamins and Herbal Agents Used for Dementia

- Vitamins
  - Vitamin E - as an antioxidant – no literature to support
- Herbals
  - Co-Q 10 – as an antioxidant
  - Ginkgo Biloba – problems with bleeding risk
  - Huperzine A - works similarly to the Cholinesterase Inhibitors)
  - Omega-3 fatty acids
    - 2 components
      - EPA – for cardiovascular → lower cholesterol
      - Docosahexaneoic acid (**DHA**) – attention and memory (maximum of 2g.day)

Medical Foods

- Caprylic acid (in Axona)
  - Medium chain fatty acid (from coconut oil)
  - Breaks down to Ketone bodies
  - Ketone bodies may be an alternative energy source for brain cells that no longer use “sugar” (glucose) as energy
  - Manufacturer stopped studies at Phase III trials

- Tramiprosate (ViviMind, Alzhemed)
  - Modified taurine (amino acid) from seaweed
  - Acts as a building block for protein
  - No benefit in dementia


Any
Questions

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