When and How to avoid Anti-psychotics in Patients with Dementia and Behavioral Symptoms

Elizabeth Eckstrom, MD, MPH*

Oregon Health & Science University

Oregon Partnership to Improve Dementia Care

***I have no disclosures**

Today’s Patients

- Mr. Smith has been hitting- especially when helped to the bathroom
- Mr. Jones is anxious, withdrawn after a hospitalization
- Mrs. Black is insisting she see her mother

Mr. Smith is having distress…

- Mr. Smith is 84 and has had dementia for several years. He lives in a memory care facility; needs help with all his ADLs except eating. His wife lives in assisted living and spends much of the day with him. Staff notes he is becoming paranoid, and Mrs. Smith admits he has hit her several times when she tries to help him to the bathroom. He is starting to fall, and team members are having a harder time getting him up. He no longer speaks in full sentences, has become incontinent, and is spitting out his food. He has lost 10 pounds in the last several months.

Why is Mr. Smith aggressive?

- You begin to examine Mr. Smith, and notice growing agitation when you examine his stomach and legs. You ask when Mr. Smith has been aggressive, and it is with toileting and transfering. You ask if he had osteoarthritis or other pain in the past, and Mrs. Smith remembers he used to complain of his back and knees. He doesn’t complain now, and he doesn’t take any pills.

Pain in Patients with Dementia

- Patients with dementia often cannot express pain; they just feel distressed and may show this by hitting, refusing ADL assistance, stopping eating
- If we don’t figure out they have pain and treat it appropriately, their distress will simply worsen

Upon Admission (or before the patient has dementia)

- Do a thorough pain history
  - Back pain?
  - Arthritis?
  - Headaches?
  - Neuropathy?
- Find out what works for their pain
  - Tylenol is best for older patients
  - Ibuprofen (caution in older adults- but safer than narcotics!)
  - Gabapentin or other nerve choices

If new distress and no clear reason for possible pain, do a careful exam

- Ears
- Mouth- sores? Ill-fitting dentures? Broken tooth?
- Arms and legs (a facility missed a broken arm!)
- Feet and hands
- Urinary retention?
- Constipation?
- UTI?

Common Sources of Pain

- Degenerative joint disease
- Spinal stenosis
- Fractures
- Pressure ulcers
- Urinary retention
- Constipation
- Peripheral vascular disease
- Post-stroke syndrome
- Improper positioning
- Fibromyalgia
- Cancer
- Contractures
- Postherpetic neuralgia
- Dental problems

Shega et al, 2007

Checklist of Nonverbal Pain

- Vocalization
- Grimace
- Bracing
- Rubbing
- Restlessness/ agitation

Pain Assessment in Advanced Dementia Scale

Items	0	1	2	Score
Breathing independent of vocalization	Normal	Occasional labored breathing, brief hyperventilation	Noisy, labored breathing, long hyperventilation, Cheyne-stokes	
Negative vocalization	None	Occasional moan or groan. Low level negative speech	Repeated troubled calling out. Loud moan/ groan. Crying	
Facial expression	Smiling or inexpressive	Sad, frightened, frowning	Facial grimace	
Body Language	Relaxed	Tense, distressed, pacing, fidgeting	Rigid. Fists clenched, knees pulled up, pulling pushing away, striking out	
Consolability	No need	Reassured by voice or touch	Unable to console, distract, or reassure	
Total score				

If you think your patient's behavior is due to pain

- Try to fix it!
  - Treat ear infection or UTI
  - Manage constipation or urinary retention
  - Ask the dentist to fit a new denture, bridge, etc
- Try non-pharmacologic strategies
  - Up and moving/ frequent position changes
  - Heating pad (hot water bottle) 20 min TID
  - Gentle massage

If you think your patient's behavior is due to pain

- Acetaminophen (Tylenol) 650 mg TID SCHEDULED
- Increase to 1000 mg TID scheduled if they seem a little better but still room for improvement
- If you notice that their pain seems to be in one location (neck, back, knees) consider:
  - Diclofenac gel (if kidney function OK)
  - Lidoderm patch

If you think your patients behavior is due to pain

- What about NSAIDs? (Ibuprofen, Aleve, etc)
  - NOT as safe as tylenol
  - Stomach, kidney, heart (BP) are main concerns
  - SAFER than narcotics
    - Fewer fractures
    - LESS acute kidney injury!
    - LESS hospitalizations and deaths!

      » *Solomon, Arch Intern Med. 2010;170(22):1968-1978*

What about NSAIDS?

- If your patient is not in kidney failure (eGFR>30 or >45 to be extra safe), doesn't have uncontrolled CHF or HTN, and hasn't had a GI bleed, may consider an NSAID
  - Naproxen (Aleve) 250 BID scheduled
  - Ibuprofen (Advil, Motrin) 400 TID scheduled
- Check kidney function after a week or two, monitor blood pressure and edema (salt restriction usually prevents edema with NSAID use)

What if these aren’t good enough?

- Fairly good “evidence” that pain is the issue (known spinal stenosis, arthritis, etc)
- Other strategies haven’t fully worked
- Patient clearly suffering/distressed
- Now is the time to try low dose opioids
  - Observe patient for times when most distressed and schedule drugs for those times (for example, 1 hr prior to ADLs or PT)
  - If distress is around the clock, schedule drugs to cover

Using Opioids

- Start low, increase gradually
- Avoid morphine if poor kidney function
- Completely avoid methadone and tramadol
- Monitor closely the first few doses- dizzy, confused, etc
- Check kidney function after a week or so
- Recheck pain scales, behaviors frequently to see if it helped- DISCONTINUE the drug if your patient does not show improvement in distress

Using Opioids- Always SCHEDULE in dementia patients

- What to start with
  - Vicodin 5/350 ½-1 tab daily- TID (watch total tylenol dosage)
  - Oxycodone 2.5 mg once daily- QID
- How quickly should I increase the dose?
  - I usually wait at least a week to do dose adjustments
- What if my patient has acute severe pain?
  - Dilaudid 1-2 mg q4-6 hrs, fentanyl patch (12.5 mg)

Back to Mr. Smith

- Hitting out when care team attempts to assist with ADLs
- History of back and knee pain
- What would you like to do?

Back to Mr. Smith

- Hitting out when care team attempts to assist with ADLs
- History of back and knee pain
- What would you like to do?
  - Daily activity, frequent position changes
  - Heating pad TID
  - Scheduled tylenol 650 mg TID, increase to 1000 TID if needed
  - Diclofenac gel before ADLs and activity (up to QID)

Back to Mr. Smith

- Hitting out when care team attempts to assist with ADLs
- History of back and knee pain
- If first steps don’t solve the problem, what next?

Back to Mr. Smith

- Hitting out when care team attempts to assist with ADLs
- History of back and knee pain
- If first steps don’t solve the problem, what next?
  - Try NSAID- aleve 250 mg BID in addition to tylenol or instead of tylenol (depending on whether you noticed any tylenol effectiveness)

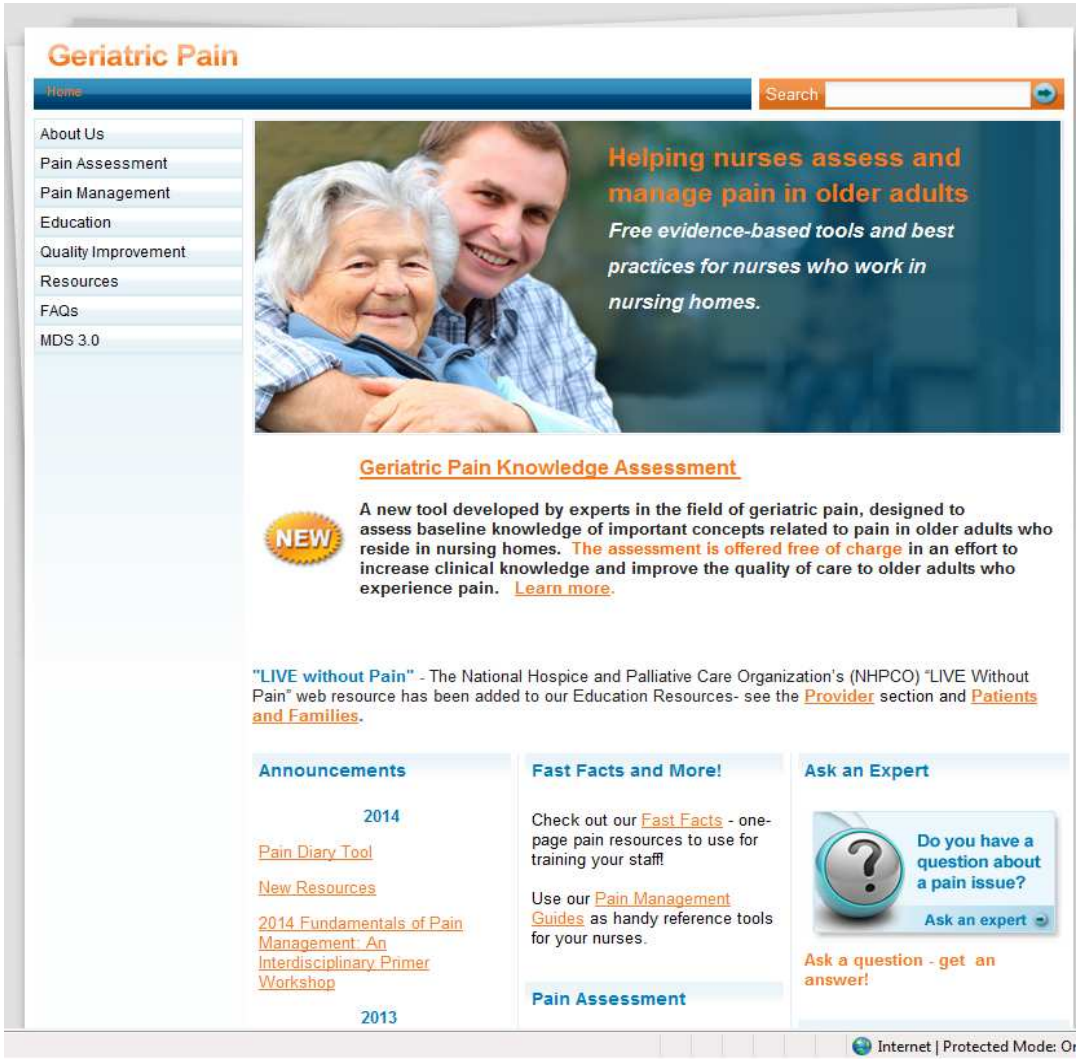
Back to Mr. Smith

- Hitting out when care team attempts to assist with ADLs
- History of back and knee pain
- If still no response, what you would like to do?

Back to Mr. Smith

- Hitting out when care team attempts to assist with ADLs
- History of back and knee pain
- If still no response, what would you like to do?
  - Vicodin ½ tab before ADLs or BID scheduled
  - OR Oxycodone 2.5 mg TID

www.geriatricpain.org



Mr. Jones, age 87, has dementia and is anxious and withdrawn after a hospitalization

Fred's issues	Fred's Meds
Probable Alzheimer's	Donepezil
CHF/CAD	HCTZ, digoxin .25 mcg daily, metoprolol, lisinopril, ASA, simvastatin
Osteoarthritis	Acetaminophen, tramadol
Insomnia	Zolpidem
Type 2 Diabetes	Metformin, glyburide
BPH	Tamsulosin
CRF- eGFR 28	

Think about Kidney Clearance- Calculate via Cockcroft Gault

Renal Clearance (ml/min)	Meds to Discontinue/Adjust Dose
GFR < 60 (CKD 3)	Dabigatran Metformin Morphine (watch for toxicity) Colchicine (dose adjust)
GFR < 40-50 (CKD 3)	NSAIDs
GFR < 30 (CKD 4-5)	Bisphosphonates HCTZ Tramadol (q 12 h, 200 mg/d max) Allopurinol (100-200 mg/d max) Memantine

And Mr. Jones got discharged on Cipro for a UTI

Drug	Dose	Considerations
Ciprofloxacin	250 mg bid, 5 to 7 days	Check INR Watch for delirium
TMP/SMZ	80/400 mg bid, 5 to 7 days	Watch kidney function; 50% if GFR < 30 Check INR; K
Nitrofurantoin (Macrobid)	100 mg bid, 5 to 7 days	**Now considered OK if GFR < 60**

Mr. Jones' Meds

Condition	Medical Treatment
Alzheimer's Disease	**Donepezil**
CHF/CAD	**HCTZ, Digoxin .25 mcg daily**, **metoprolol,** lisinopril, **ASA, simvastatin**
Osteoarthritis	Acetaminophen, **tramadol**
Insomnia	**Zolpidem**
Type 2 Diabetes	**Metformin**, **glyburide, finger sticks**
BPH	**Tamsulosin**

Drugs most likely to cause delirium

- *Anticholinergics* (e.g., diphenhydramine), TCAs (e.g., amitriptyline, imipramine), antipsychotics
- Anti-inflammatory agents, including prednisone
- Benzodiazepines or alcohol — acute toxicity or withdrawal
- Cardiovascular (e.g., digitalis, antihypertensives)
- Diuretics
- Histamine blockers (e.g., cimetidine, ranitidine)
- Lithium
- Opioid analgesics

Medication/Substance Withdrawal syndromes

- Clozapine, Paxil, alcohol are biggest offenders

Anticholinergic properties frequently overlooked:

Elavil (amitriptyline)
Cogentin (benztropine)
Bentyl (dicyclomine)
Ditropan (oxybutynin)
Detrol (tolterodine)
Benadryl (diphenhydramine)
Zyprexa (olanzapine)
Levsin (hyoscyamine)

Flexeril (cyclobenzaprine)
Atarax/Vistaril(hydroxyzine)
Welbutrin/Zyban (bupropion)
Antivert (meclizine)
Ipratropium (atrovent)
Phenergan (promethazine)
Atropine
Quinidine

What should you use instead?

- Nausea- suggestive evidence that ondansetron is better
- Sleep- No drugs are truly safe in older people
  - Back rub, warm milk, relaxing music
  - Rozerem may help sleep/wake cycle
  - Trazodone mildly anticholinergic, try 12.5-25 mg
- Pain- already covered
- GI prophylaxis: ONLY PPIs (shorted course possible)
- Sertraline or citalopram

Mr. Jones' Meds

Condition	Medical Treatment
Alzheimer's Disease	**Donepezil-dose reduced**
CHF/CAD	**metoprolol,** lisinopril, (stopped ASA,, simvastatin, HCTZ, Digoxin .25 mcg)
Osteoarthritis	Acetaminophen, stopped tramadol
Insomnia	Stopped Zolpidem
Type 2 Diabetes	Stopped Metformin, glyburide, finger sticks
BPH	Stopped Tamsulosin

Mrs. Black is insistent…

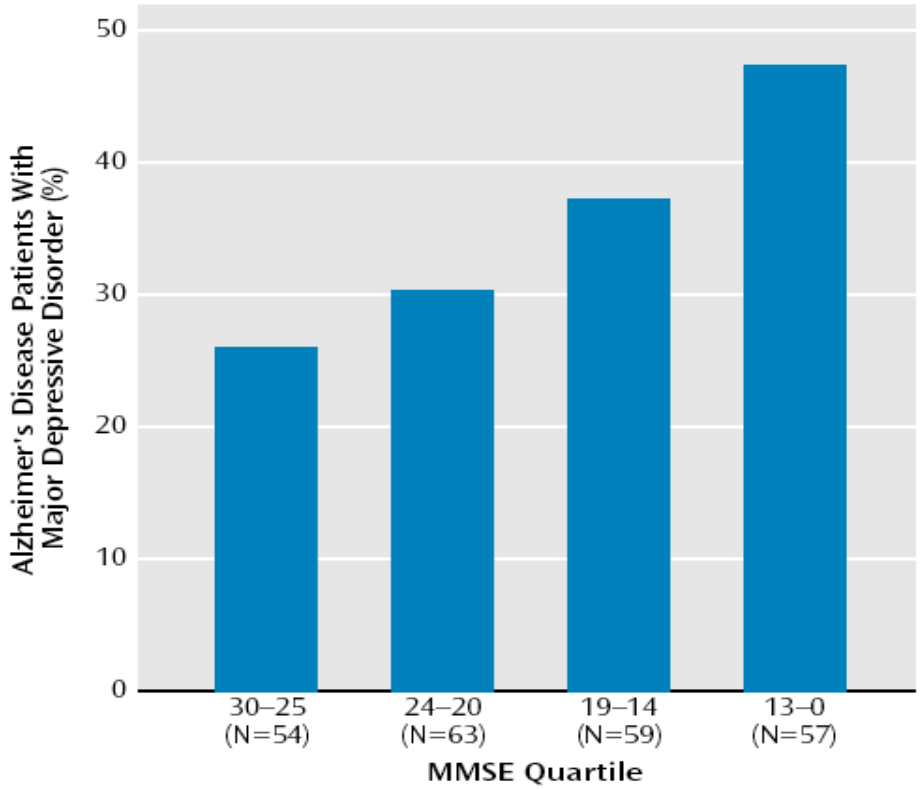
- Mrs. Black is 89 and has had dementia for about 10 years. Her husband continues to care for her at home, but lately has become increasingly concerned about her. She has been demanding her mother, and bursts into tears when Mr. Black tells her that her mother is dead. She has been refusing to eat, and is starting to wander at night.
- What do you think is going on?

Prevalence of Major Depressive Disorder in Alzheimer Disease

Zubenko GS et al. Am J Psych 2003; 160: 857-866

High prevalence rates with increasing prevalence in more severe AD.

FIGURE 1. Major Depressive Disorder Onset at or After the Onset of Cognitive Impairment in Alzheimer's Disease Patients by Level of Dementia Severity[a]



[a] Rates for decreasing MMSE quartiles were 25.9%, 30.2%, 37.3%, and 47.4%, respectively.

Depression

- Are there other symptoms of depression?
  - Depressive symptoms are more common than major depression
  - Apathy is very common
  - Anxiety, guilt, hopelessness and suicidality can help differentiate from apathy
  - Consider using the GDS
  - Cornell Scale for Depression in Dementia

NAME _____ AGE_____ SEX_____ DATE _____

Cornell Scale for Depression in Dementia

Ratings should be based on symptoms and signs occurring during the week before interview. No score should be given if symptoms result from physical disability or illness.

SCORING SYSTEM

a = Unable to evaluate **0 = Absent**

1 = Mild to Intermittent **2 = Severe**

Score greater than 12 = Probable Depression

A. MOOD-RELATED SIGNS

	a	0	1	2
1. Anxiety; anxious expression, rumination, worrying				
2. Sadness; sad expression, sad voice, tearfulness				
3. Lack of reaction to pleasant events				
4. Irritability; annoyed, short tempered				

B. BEHAVIORAL DISTURBANCE

	a	0	1	2
5. Agitation; restlessness, hand wringing, hair pulling				
6. Retardation; slow movements, slow speech, slow reactions				
7. Multiple physical complaints (... if not included above)				

Depression in Dementia

- A number of negative trials recently- suggesting a 3 month trial of non-drug interventions and reassess
- Most of us who are seeing these patients and note a CHANGE in symptoms affecting quality of life and caregiver stress will initiate an SSRI
  - Sertraline, start at 25 mg, titrate q2 weeks to 100 mg if needed
  - Citalopram, start at 10 mg, titrate in 2 weeks to 20 mg if needed

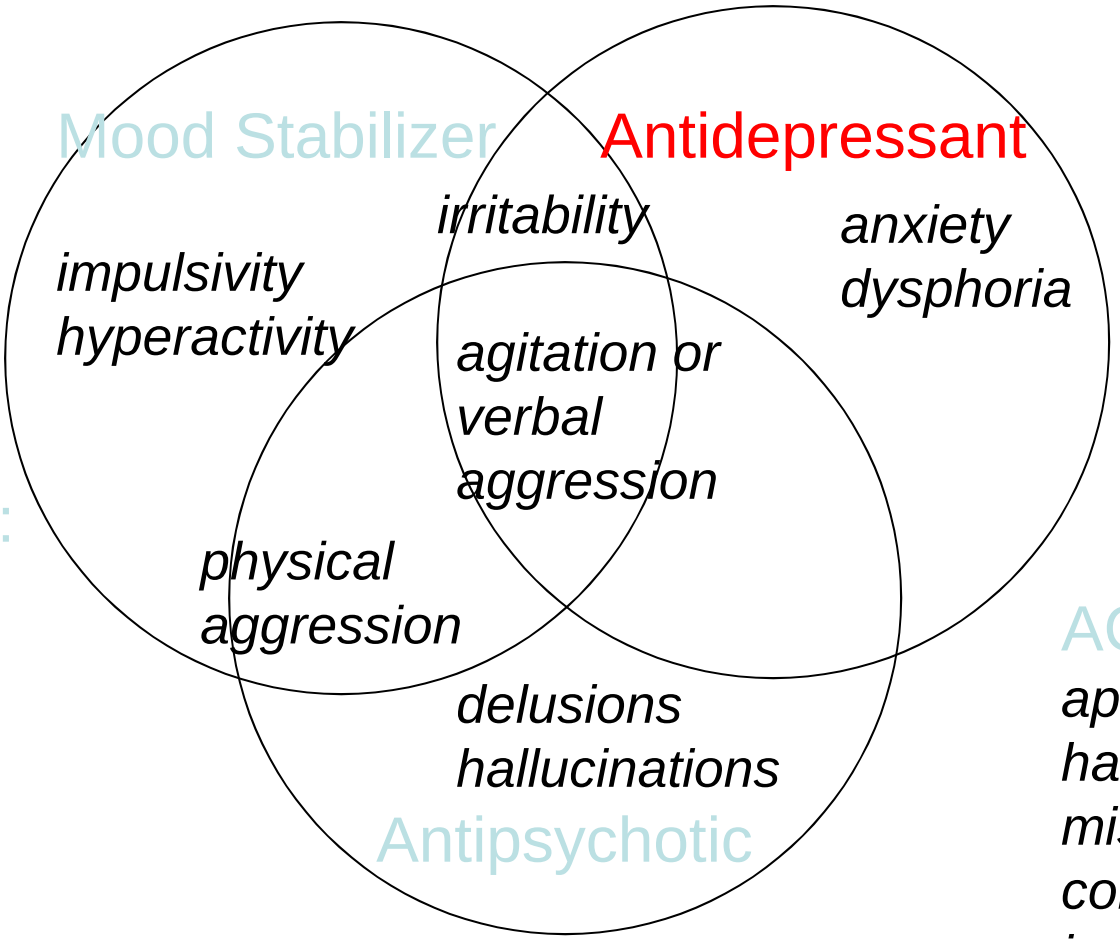
Which symptoms respond best to medications?

- Responsive to Meds
  - Anxiety
  - Irritability/anger
  - Delusions
  - Hallucinations
  - Insomnia
  - Agitation/aggression
  - Hyperactivity
  - Dysphoria
  - Apathy
- Less responsive to Meds
  - Perseverative yelling
  - Pacing
  - Exit seeking
  - Wandering
  - Disrobing
  - Sexual impulsivity

A Note on Medication

- SSRI's are going to require a trial of at least 2 weeks or longer
- Antipsychotics, trazodone – should see response in a few days
- If your patient seems to be depressed, but is having acute distress, you may need a BRIEF course of a more rapidly acting medication to help relieve distress while the SSRI is "kicking in"

Symptomatic Approach



Analgesic:

restless
calling out
grimacing
combative

AChI:

apathy
hallucinations
misperceptions
confusion
inattention

Summary

- When a patient with dementia is “agitated,” think about pain, drug side effects/ interactions, and depression as likely reasons for the agitation.
- NONE of these patients (or others like them) should receive antipsychotics
- Treating underlying etiologies is much more effective than treating symptoms with an antipsychotic!

Questions?