Management of BPSD

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Outline-Managing BPSD

- The Problems, The Challenges, The Beliefs
  - Complex clinical process, provider/payor/systems
  - Hugh cost, Mega-Dollars, Impact high numbers
  - Changing Beliefs and Culture
- General Management Concepts-Four
  - Behavior…….Problem-solving
  - Simplify……Drug
- The Evidence……or lack of evidence

Behavioral and Psychological Symptoms of Dementia BPSD

- Symptoms affect up to 90 percent of individuals with dementia at some stage
  - Apathy, depression, psychosis, aggression, agitation, anxiety, and wandering
  - Patient and caregiver distress
  - Accelerated functional and cognitive decline
  - Leading predictors of institutionalization
  - Challenge staff in long-term care (LTC) facilities
  - LTC estimated 80 percent of the residents with dementia experience some degree of behavioral and psychological symptoms.

http://www.effectivehealthcare.ahrq.gov/ehc/index.cfm/search-for-guides-reviews-andreports/?pageAction=displayTopic&topicID=559

Complex Med Use in Elderly

- Frail with multiple medical conditions
  - CV, arthritis, stroke, diabetes
- Half >85 years disabling dementia
  - impairs ability to communicate, ADL
- Average 7 to 15 medications
  - High risk medication-related problems
- Poor LTC prescribing quality
  - Well documented, one of most difficult to improve

Tjia J, et al, Am J Geriatr Pharmacother. 2012 Feb; 10(1):37-46. doi:10.1016/j.amjopharm.2011.12.005.

High Use/Cost Antipsychotics in LTC

- 25-33% LTC residents US on antipsychotic
  - Affects 390,000 frail, institutionalized elderly
  - Wide geographic variation US-up to 45%

- 2006-most costly drug class Medicaid reimbursement
  - $176 Million dual eligibles AND
  - $2.6 Billion nondual eligibles

Chen Y, et al. Arch Intern Med. 2010; 170:89–95. [PubMed: 20065204]
Mathematica Policy Research Institute. CMS; 2010. Exhibit 21.
IMS Health. 2007 Top Therapeutic Classes by US Sales. 2008

Inappropriate Antipsychotics in LTC

- 80% antipsychotics off-label, mainly BPSD
- 2006 in US LTC resident with dementia
  - 22.6% without behavioral symptoms
  - 29.5% with non-aggressive behavioral symptoms
  - 51.2% with aggressive behavioral symptoms
- 21% US LTC residents receive antipsychotic without a psychosis-related diagnosis

Chen Y, et al. Unexplained variation across US nursing homes in antipsychotic prescribing rates. Arch Intern Med. 2010; 170:89-95. [PubMed: 20065204]
Crystal S, et al. Broadened use of atypical antipsychotics: safety, effectiveness, and policy challenges. Health Aff. 2009; 28:w770-w781.

Centers Medicare and Medicaid

22% antipsychotic prescriptions in nursing homes are problematic per CMS standards, OIG 2011 Report

Problem per CMS standards	% of Claims
Excessive dose	10.4%
Excessive duration	9.4%
Without adequate indication	8.0%
Without adequate monitoring	7.7%
In the presence of adverse effects that indicate the dose should be reduced or discontinued	4.7%

Office of Inspector General 2011 http:oig.hhs.gov/oei/reports/oei-07-08-00150.pdf. Accessed 8/23/2014

Senate Special Committee on Aging Hearing 11/30/11

"Overprescribed: The Human and Taxpayers' Costs of Antipsychotics in Nursing Homes"

Statements from Senator Herb Kohl:

- *"While antipsychotic drugs have been approved by the FDA to treat an array of psychiatric conditions, numerous studies have concluded that these medications can be harmful when used by frail elders with dementia who do not have a diagnosis of serious mental illness……. Improper prescribing not only puts patients' health at risk, it also leads to higher health costs."*

FDA Black Box Warning

- Issued in 2005
- **Warning: Increased Mortality in Elderly Patients with Dementia-Related Psychosis**
  - Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. [Name of Antipsychotic] is not approved for the treatment of patients with dementia-related psychosis.

Pharmaceutical Industry Antipsychotics Big Business…….Really BIG

IMS Health. Top Therapeutic Classes by US Sales.

Department of Justice

Criminal & Civil Penalties Illegal Marketing

- Johnson & Johnson-November 2013
  - $2.2 Billion Risperdal, Invega Dementia
- AstraZeneca-April 2010
  - $520 Million Seroquel Insomnia, Dementia
- Eli Lilly-January 2009
  - 1.4 Billion Zyprexa Dementia

http://www.usdoj.gov/usao/pae/News/Pr/2009/jan/lillyinfo.pdf
Mann M. ABA Health eSource. 2009 March; 5(7).
http://www.justice.gov/opa/pr/2013/November/13-ag-1170.html
http://www.justice.gov/opa/pr/2010/April/10-civ-487.html
Accessed August 26, 2014.

Primary Challenge is Changing Beliefs Changing Expectations, Changing Culture

- Most health care professionals and families believe
- (1) dementia "behaviors" are abnormal, need to be treated, with a drug
- (2) medications are effective in dementia behaviors
- (3) antipsychotics have a few side effects, but safe to use
- (4) harmful to attempt to reduce dose or discontinue; behaviors will be worse and next time the medication won't work

Tjia J et al, *Am J Geriatr Pharmacother*. 2012 February ; 10(1): 37–46. doi:10.1016/j.amjopharm.2011.12.005.

Knowledge of and perceived need for evidence-based education about antipsychotic medications among nursing home leadership and staff

- Design: Survey of leadership and direct care staff of nursing homes in Connecticut was conducted in June 2011.
- Results: A total of 138 nursing home leaders and 779 direct care staff provided useable questionnaires
- Only 24% of nursing home leaders identified at least 1 severe adverse effect of antipsychotics; 13% of LPNs and 12% of RNs listed at least 1 severe adverse effect. Fifty-six percent of direct care staff believed that medications worked well to manage resident behavior. Leaders were satisfied with the training that staff received to manage residents with challenging behaviors (62%). Fifty-five percent of direct care staff felt that they had enough training on how to handle difficult residents; only 37% felt they could do so without using medications.
- Conclusions: Findings suggest that a comprehensive multifaceted intervention designed for nursing homes should aim to improve knowledge of antipsychotic medication risks, change beliefs about appropriateness and effectiveness of antipsychotics for behavior management, and impart strategies and approaches for nonpharmacologic behavior management

Lemay CA et al, J Am Med Dir Assoc. 2013 Dec;14(12):895-900.
doi: 0.1016/j.jamda. 2013. 08.009. Epub 2013 Sep 24

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  - Behavior…….Problem-solving
  - Simplify/Symptom……Drug
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Management of BPSD

- Behavior or Unmet Need; Basics First
  - Pain, Constipation
- Problem solve Cause of Behavior
  - Drug-Induced ‘Behaviors’
- Simplify; Symptom Clusters
  - Optimize current regimen
  - Caregiver Factor
- Drug Therapy
  - Evidence Based Efficacy & Side effects
  - Withdrawal
  - Psychosocial interventions

General Concepts 1
Behavior or Unmet Need?

- Basics First: hot, cold, hungry, thirsty, tired, bored, toileting, pain…….

- Pain Undertreated in Demented Elderly

- Constipation Over and Undertreated

Pharmacologic Approaches to Agitation: Appropriate Pain Management

- Study from September 2011: "Efficacy of treating pain to reduce behavioral disturbances in residents in nursing homes with dementia: cluster randomised clinical trial"[5]
- 352 nursing home residents with moderate to severe dementia and clinically significant behavioral disturbances randomized to receive either a stepwise protocol for pain treatment for 8 weeks or usual care
- Stepwise pain protocol included acetaminophen, morphine, transdermal buprenorphine, or pregabalin
- Primary outcome measure was agitation, while secondary outcomes were aggression, pain, ADL's and cognition.

[5]Husebo BS, Ballard C, Sandvik R et al. *BMJ* 2011;343:d4065 doi: 10.1136/bmj.d4065

Pharmacologic Approaches to Agitation: Appropriate Pain Management (cont'd)

Study Results

- Agitation was significantly reduced compared to control group at 8 weeks
- Significant benefit for aggression, overall severity of neuropsychiatric symptoms, and pain
- No significant differences in ADL's or cognition

Conclusion

"A systematic approach to the management of pain significantly reduced agitation in residents of nursing homes with moderate to severe dementia. Effective management of pain can play an important part in the treatment of agitation and could reduce the number of unnecessary prescriptions for psychotropic drugs in this population"[5]

[5]Husebo BS, Ballard C, Sandvik R et al. *BMJ* 2011;343:d4065 doi: 10.1136/bmj.d4065

PRN Pain Medications in a Demented Elderly

Constipation-Over and Undertreated

- Why 3 drugs, when one effective will work?
- Why PRN meds, when resident can not remember if they had a BM or not?
- Docusate (Surfak, Colace)-not effective
- Fiber (all types)-effective for diarrhea
- Any medication that has to be mixed and taken with glass of fluid, eg PEG (Miralax)-not effective due to noncompliance
- Senna-effective
- Opioid-more Senna, max is 8 tablets daily

General Concepts 2
Problem-solve cause of Behavior

- Four D's
  - Delirium, Dementia, Depression, Drug
- Often Multifactorial and Comorbid Conditions
- Dementia and/or Depression Baseline with
  - Episodic Delirium
  - Drug-induced behaviors/side effects
  - Various degrees and durations

Can Drugs Cause Behaviors?

- Mental Status Change-think drug
  - Sedation: Antipsychotics, BZD, Antihistamines, Narcotics, Mood Stabilizers, Hypnotics…
- Delirium-think drug
  - Hallucinations, psychosis: levodopa (Sinemet), Digoxin, Benadryl, Antibiotics, analgesics (Percocet, Morphine)……..
- Agitated, Restless, Pacing-think drug
  - Akathisia: antipsychotics
  - Serotonin Syndrome: SSRI, tramadol

https://www.youtube.com/watch?v=47-w494maK8

Akathisia

- https://www.youtube.com/watch?v=47-w494maK8

General Concept 3
Simplify Symptom Clusters

- Simplify medication regimen
  - Key to eliminate as many possible drug-induced causes of behavior as possible
  - Optimize current psychoactives
- Symptom Clusters
  - Anxiety and/or Depression
  - Problematic Psychosis (paranoia, hallucinations, delusions)
  - Harmful/Dangerous/Extremely Distressing Behaviors

Symptom Clusters

Symptom Cluster	Medication	Limited Time Periods
Irritable ,agitation , insomnia, pacing DX: Anxiety and/or Depression Mild Moderate Severe	1-SSRI antidepressant --Avoid paroxetine --Order titration: escitalopram 10 mg PO 7 d; then 20 mg daily 2-Individualize: duloxetine, buspirone, trazodone, etc	BZD Overlap -lorazepam 0.5 mg BID-QID hitting/anxious X 3-30 days Acute -lorazepam 0.5-1.0 mg IM now Avoid anticholinergics: -hydroxyzine, -diphenhydramine
Psychosis **Distressing** Hallucinations, Delusions **Dangerous** Aggression	1-Antipsychotic -Risperidone 0.5-1.0 mg PO q12h -Reevaluate 7 d, 4 wk, q3mo	No Role for PRN Antipsychotic in LTC setting -haloperidol 1 mg IM now

BPSD Specific Types of Dementia

- Parkinson's Disease or Lewy Body Dementia
  - Tolerate antipsychotics poorly
  - Psychosis: decrease antiparkinson med doses
  - Questionable benefit any treatment
  - Falls and orthostasis
  - Clozapine, quetiapine least causative EPS

- Frontotemporal Dementia-mixed data, preliminary
  - Trazodone, Stimulants, Paroxetine

Weintraub and Hurtig, 2007;164:1491-8. Huey et al, J Clin Psychiatry 2008;69(12):1981-2.
Deakin et al, Psychopharmacology 2003;10:10. Moretti et al, Eur Neurol 2003;49:13-9.

General Concept 4
Drugs for BPSD

- Evidence-Based Scientific Research and Consensus of Experts in Psychiatry and Geriatrics
  - Efficacy of medications is none to modest
  - Serious side effects, including death
- Caregiver Factor
- Reassess continued need frequently, at least every 3 months; more often initially/delirium
- Taper and discontinue is safe and needs to be attempted frequently

Caregiver Factor

General Concepts Management

- B Behavior or Unmet Need?
- P Problem solve cause of behavior (4 D's)
- S Simplify Symptoms
- D Drugs no/minimal effective; serious SE

Educate, Inform, Consent

- **What are antipsychotic medicines*?**

These medicines can help when people see or hear things, or believe things that are not true. But they can also have side effects (things that come from taking a medicine but are not part of the treatment). These medicines may cause a small increase in the risk of death. So it's important to only use them when needed. And only if they help. Other ways to handle problems with dementia should be tried first.

- **What are the possible benefits of antipsychotic medicines?**

They may help aggressive behavior, hallucinations, or delusions. This can make a person with dementia feel better. It might also make it safer for the person or others.

- **What will these medicines NOT help?**
- Antipsychotic medicines do not help these problems:
- **Not being social**—when a person doesn't want to be friendly to others
- **Not taking care of their self**
- **Memory problems**
- **Not paying attention or caring** about what is going on around them
- **Yelling or repeating questions** over and over
- **Being restless**—when it's hard for a person to sit still

- There may be other medicines or ways to help. So talk to the health care team.

- **Making the Choice**

- Sometimes, no matter what you do, a person with dementia may be aggressive or have bad hallucinations or delusions. Medicine might help if the person is acting dangerous or is very upset, and nothing else is working. It may help the person feel better, even if there are risks. Think about things like:

- What would the person have wanted before they got dementia?

- What would they want if they knew they were biting, hitting, or kicking people?

- If the person is having scary hallucinations or seeing people who aren't there, would they want it to stop if a medicine might help?

- Many people would want to stop these things if possible, even if there are risks.

- Deciding to use an antipsychotic medicine is hard. There are risks. Not everyone is helped. But many people can take them and not get side effects.

- We can't cure dementia. When it is getting worse, you can think about whether using an antipsychotic medicine makes a person's comfort and quality of life better, even if there are risks.

Medications for BPSD

Medications Studied To Date

- Antidepressants-SSRI, trazodone, mirtazapine
- Mood Stabilizers-divalproex, carbamazepine
- Antianxiety-benzodiazepines (lorazepam), buspirone
- Cognition Enhancers-AChI (donepezil, ravastigmine), memantine
- Miscellaneous-estrogen, prazosin, propranolol
- Antipsychotics

Evidence Based Medicine

- Limited research
- No or minimal effective
- Antipsychotics have most evidence of efficacy in psychosis and aggression
- Antipsychotics increase risk stroke and death
- All may have significant SE
  - Cognition, falls, weight, sedation, function

Medication Effectiveness in BPSD

- Antipsychotic orally effect takes 3-7 days to start working
  - Very sedating medication so acute effect is most likely due to sedating effect not the antipsychotic effect
- Randomized controlled trial (RCTs) is the gold standard method
- Meta-analysis is method that combines the results from multiple RCTs

Salzman C et al. *J Clin Psychiatry*. 2008 June ; 69(6): 889–898.

Antipsychotic Evidence Effectiveness in BPSD is weak Meta-Analysis (JAMA 2011)

- Olanzapine, Risperidone and Aripiprazole, had a small but statistically significant effect (12 – 20% got better) when compared to placebo
- Quetiapine did not have a statistically significant effect
- Antipsychotics led to an average change/difference on the NeuroPsychiatric Inventory (NPI) of
  - 35% from a patient's baseline
  - 3.41 point difference from placebo group

  (note: a 30% change and 4.0 difference is the minimum threshold needed for a clinically meaningful result)
- No conclusive evidence was found regarding the comparative effectiveness of different antipsychotics

Source: JAMA 306:1359-69 2011; Meta-analysis 38 RCTs in dementia

Antipsychotic Effectiveness in Treating Aggression in Dementia (Cochrane Review 2012)

- Evaluated 16 randomized controlled trials with atypical antipsychotics vs placebo although only 9 had sufficient data to include in meta-analysis.
- Conclusions:
  - Statistically significant improvement in aggression with risperidone and olanzapine when compared to placebo
  - Statistically significant improvement in psychosis with risperidone
  - Significant increase in drop-outs in risperidone (2 mg) and olanzapine (5-10 mg) treated patients

Source: Cohcrane Review 2012; Meta-analysis 16 RCTs in dementia

Effectiveness of Antipsychotics in Dementia

Drug	% improvement in symptom scale	% treatment discontinuation
Olanzapine	32%	24%
Quetiapine	26%	16%
Risperidone	29%	18%
Placebo	21% (p=0.22)	5% (p=.009)

Source: Scheurer D. Antipsychotic use in Primary care: limited benefit, sizable risk
Independent Drug Information Service (IDIS) 2012.

Dose for Antipsychotics Used in BPSD

Medication	Low Dose	Normal Dose
Aripiprazole	<2 mg/d	10-30 mg/d
Olanzapine	<5 mg/d	5-20 mg/d
Quetiapine	<50 mg/d	300-800 mg/d
Risperidone	<1 mg/d	4-16 mg/d

Antipsychotic Effectiveness with Low Dose

- Low dose Risperidone (<1 mg/d) has small positive effect but also has increase risk of adverse events
- Low dose Olanzapine (5 mg/d) has no positive effect but does have increase risk of adverse events
- Low dose Aripiprazole and Quetiapine effectiveness are unknown
- Quetiapine at normal dose ineffective

Source: Cochrane Review 2012; Meta-analysis 16 RCTs in dementia

Odds of having an adverse event after receiving Risperidone 1 mg/d compared to placebo

Adverse Event	Odds Ratio
Mortality	1.25
Somnolence	2.40
Falls	0.84
Extrapyramidal SE	1.78
UTI	1.40
Edema	2.75
Abnormal Gait	5.31
Urinary Incontinence	13.6
Stroke	3.64
Drop out (had to stop meds)	1.43

Cochrane Review 2012; Meta-analysis 4 RCTs in dementia

Odds of having an adverse event after receiving Olanzapine 5 – 10 mg/d compared to placebo

Adverse Event	Odds Ratio
Mortality	2.31
Somnolence	3.72
Falls	1.52
Abnormal Gait	4.76
Urinary Incontinence	9.60
Stroke	5.24
Drop outs (had to stop med)	3.34

Cochran Review 2012; Meta-analysis 3 RCTs in dementia

Elderly with Dementia-Related Psychosis

- Antipsychotic treatment increased risk of death compared to placebo
- Consistent across all antipsychotics
  - First generation
  - Second generation (Atypical)
- Relative risk = 1.6 to 1.7
  - Absolute risk = 3.5% vs 2.3% with placebo
- Number Needed to Harm = 83
  - Number need to treat = 5 to 14
  - For every 9 to 25 persons helped, 1 death associated

Jeste et al, Neuropsychopharmacology 2008;33:957-70.
Huybrechts et al, BMJ 2012; 344:e977.
Maher A and Theodore G, JMCP 2012;18:No.5-b.

Net Effectiveness

"For every 100 patients with dementia treated with an antipsychotic medication,

only 9 to 25 will benefit and 1 will die"

Drs Avorn, Choudhry & Fishcher

Harvard Medical School

Dr Scheurer

Medical University of South Carolina

Source: Independent Drug Information Service (IDIS) Restrained Use of antipsychotic medications: rational management of irrationality. 2012

Antipsychotic Withdrawal to Continuation in Dementia

- Nine randomized, placebo controlled trials: 606 participants
- Setting: Nursing Homes (7), Outpatient (1), Both (1)
- Primary efficacy outcomes
  - success of withdrawal (i.e. remaining in study off antipsychotics)
  - NPS scores

- No overall significant difference between groups on the primary outcomes in 8 of 9 trials

Declercq T et al, Cochrane Database Syst Rev. 2013 Mar 8;3:CD007726. doi: 10.1002/14651858.CD007726.pub2.

Withdrawal Antipsychotics BPSD Psychosis/Agitation Responders

- Haloperidol-one pilot study
  - time to relapse was significantly shorter in the discontinuation group (Chi(2) = 4.1, P value = 0.04)
- Risperidone 4-8 months, one study
  - increased risk of relapse in discontinuation group, that is, increase in the Neuropsychiatric Inventory (NPI)-core score of 30% or greater (P value = 0.004, hazard ratio (HR) 1.94, 95% confidence interval (CI) 1.09 to 3.45 at four months)

Declercq T et al, Cochrane Database Syst Rev. 2013 Mar 8;3:CD007726. doi: 10.1002/14651858.CD007726.pub2.

Withdrawal Antipsychotics BPSD

- Pooled outcome: full NPI-score, used in two studies
  - No significant difference between people withdrawn from and those continuing on antipsychotics at three months (mean difference (MD) -1.49, 95% CI -5.39 to 2.40). These two studies reported subgroup analyses according to baseline NPI-score (14 or less versus > 14). In one study,
  - Baseline NPI 14 or less, one study
    - DC group significantly less agitated three months(NPI-agitation, Mann-Whitney U test z = 2.4, P value = 0.018)
  - Baseline NPS >14, two studies
    - DC group significant behavior deterioration (Chi(2) = 6.8; P value = 0.009 for the marked symptom score in one study).

Declercq T et al, Cochrane Database Syst Rev. 2013 Mar 8;3:CD007726. doi: 10.1002/14651858.CD007726.pub2.

Psychosocial interventions Vs Usual Care Reduce Antipsychotics

- Four randomized controlled trials in care homes
- Interventions
  - Education and training for nursing staff
  - multidisciplinary team meetings (1)

- Decrease of the proportion of residents using antipsychotic OR
- Reduction in days with antipsychotic use

Richter T et al, Cochrane Database Syst Rev. 2012 Dec 12;12:CD008634. doi: 10.1002/14651858.CD008634.pub2.

Management of Neuropsychiatric Symptoms of Dementia: Some Key Points

- "Medication treatment of behavioral disturbances of dementia is of limited efficacy and should be used only after environmental and nonpharmacologic techniques have been implemented"

- "No psychoactive medication prescribed to treat neuropsychiatric symptoms of dementia should be continued indefinitely, and attempt at drug withdrawal should be made regularly (e.g., every 3-6 months)"

- "The goal (of treatment) is reduction, rather than elimination, of the distressing behavior…"

American Geriatrics Society. A Guide to the Management of Psychotic Disorders and Neuropsychiatric Symptoms of Dementia in Older Adults.
April 2011. Available at http://www.americangeriatrics.org/; accessed 8/3/2011

References Available Upon Request:
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