Welcome to the Medication Safety Community of Practice Webinar Series

Hosted by ISMP Canada
March 21, 2012

Opportunities for Quality Improvement:
Contemporary Issues in the Use of Psychotropic Medications in the Management of Behavioural and Psychological Symptoms of Dementia in Long-Term Care
Medication Safety CoP Aim

- To improve Medication Safety within Long Term Care homes. It is a collaboration of three organizations HQO, QHN and ISMP Canada with support from SHRTN

Medication Safety CoP Team

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- You are on Mute right now but we can open the audio lines later for questions, so it’s important that you joined the call correctly.

- There is a Chat box function that you can use (address your questions to “All Panelists”).
Opportunities for Quality Improvement:
Contemporary Issues in the Use of Psychotropic Medications in the Management of Behavioural and Psychological Symptoms of Dementia in Long-Term Care

Presenter

- Carlos Rojas-Fernandez, BSc (Pharm), PharmD
- Schlegel Research Chair in Geriatric Pharmacotherapy
- Schlegel-UW Research Institute on Ageing & School of Pharmacy, University of Waterloo
Objectives

- Increase awareness of medication use issues in the management of behavioural and psychological symptoms (BPSD) in long-term care (LTC) residents.
- Increase knowledge of improvement opportunities in LTC medication management system that affects physicians, nurses, pharmacists, and ultimately residents.
- Highlight actions that each profession can take to enhance the safety and care of residents with BPSD.
Disclosures

- Current funding:
  - UW-RBJ Schlegel RIA
  - CIHR
  - Pfizer
  - Purdue
  - AstraZeneca
Roles

- **Research**
  - Long term care and primary care
    - Alzheimer’s disease and related disorders, falls
    - Various other diseases

- **Clinical Geriatric Pharmacotherapy**
  - CFFM Memory Clinic

- **Teaching**
  - UW School of Pharmacy
  - AHS Health Studies & Gerontology
  - MacMaster Family Medicine

Questions

- >50%-90% of patients with dementia will be affected by BPSD.
  - True or false?

- BPSD are best treated with medications
  - True or false?

- When medications are necessary for BPSD, any of the antipsychotics may be used interchangeably.
  - True or false?
Questions

• In many cases, BPSD may be the result of reversible causes.
  – True or false?

• When drugs are used to manage BPSD, what is the optimal duration of therapy?
  – 6 months
  – 3 months
  – 9 months
  – 12 months
  – 24 months

Symptomatic expression of dementia

[Diagram showing the relationship between Cognition, Behavior, Function, and a Unique Symptom Pattern of AD]
Symptom Complexes of BPSD

- Apathy
- Psychosis
- Depression
- Inappropriate sexual behaviours
- “Agitation”
- Altered circadian

Relevance of BPSD

- >50%-90% of patients are affected
- Reduced ADL function (incl. incontinence)
- Compromised nutrition and hydration
- Falls, aspiration, injuries
- Suffering, excess disability
Relevance of BPSD

- Caregiver time, stress, depression.
- Increased hospitalizations.
- Premature institutionalization.
- Overall ↑ in health care use (e.g., ER visits, ALC time).
- Interference with medical and nursing care.

Symptom Complexes of BPSD

- Apathy
- Psychosis
- Depression
- Inappropriate sexual behaviours
- “Agitation”
- Anxiety
- Altered circadian
Apathy

• Is a behavioural sign of executive dysfunction.
• May be characterised by loss of motivation:
  – Reduced initiative
  – Poor persistence
  – Lack of interest
  – Indifference
  – Blunted emotional response, lack of concern
  – Low social engagement

• Compare w depression:
  – Negative thoughts, dysphoria, pessimism, self criticism

• One of the most commonly occurring BPSD (up to 92% of AD patients).

• Increases care demands, CG burden and stress.
## Psychosis: AD Vs Schizophrenia.

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<tr>
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<th>Psychosis of AD</th>
<th>Schizophrenia</th>
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<tbody>
<tr>
<td>Bizarre or complex delusions</td>
<td>Rare</td>
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<td>Misidentifications of caregivers</td>
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<td>Common form of hallucinations</td>
<td>Visual</td>
<td>Auditory</td>
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<td>Active suicidal ideation</td>
<td>Rare</td>
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<tr>
<td>Past history of psychosis</td>
<td>Rare</td>
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### Delusions

- Theft
- House is not one’s home
- CG or spouse is impostor
- Abandonment
- Infidelity
Depression in AD.

- Depressive symptoms often fluctuate.
- Depressed patients with AD exhibit more self-pity, rejection sensitivity, anhedonia and psychomotor disturbance than depressed older patients without dementia.
- Major depression in AD is associated with an increased mortality rate, but no acceleration of cognitive decline.

Inappropriate sexual behaviours

- Up to 25% of patients with dementia exhibit these behaviours
- Non-pharmacological approaches very important:
  - Education
  - Avoid confrontation
  - Distraction,
  - Modified clothing, etc
Circadian Rhythm Disturbances

- Functional and anatomic changes occur in the suprachiasmatic nucleus in dementia.
- Alterations of the daily rhythm of serum melatonin have been correlated to some cases of sleep disturbances in Alzheimer’s disease.

Circadian Rhythm Disturbances

- Disturbances of sleep and day-night reversals are common.
- Sleep disturbances may be more common in VaD, DLB & PSP, compared to those found in AD.
Agitation

- Some symptoms don’t fit well into defined symptom complexes of BPSD such as psychosis, depression or anxiety.

- They are consigned to the “grab-bag” category of “agitation”, which is a sensitive, but non-specific term.

- Agitation
  - May be defined as inappropriate verbal, vocal or motor activity that is not judged by an outside observer to result directly from the needs or confusion of the person.

Physically Non-Aggressive

- General Restlessness
- Repetitive mannerisms
- Pacing
- Hiding Objects
- Inappropriate Handling
- Shadowing
- Escaping protected environment
- Inappropriate Dressing/Undressing

Verbal Non-Aggressive

- Negativism
- Chanting
- Repetitive Sentences
- Constant Interruptions
- Constant Requests for Attention
**Physically aggressive**

- Hitting
- Pushing
- Scratching
- Grabbing
- Kicking
- Biting
- Spitting

**Verbally aggressive**

- Screaming
- Cursing
- Temper Outbursts

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**Aggression symptom complexes include:**

- Reactive aggression associated with personal care, discomfort.
- Aggression associated with delirium
- Aggression associated with depression
- Aggression associated with psychosis
- Spontaneous disinhibited aggression
Anxiety Symptoms in BPSD

- No specific definition of anxiety in BPSD is available;
- Generalized anxiety disorder type symptoms
- Godot syndrome (repeatedly asking questions on a forthcoming event)
- Fear of being left alone
- Pacing
- Wringing of hands, fidgeting
- Chanting

Peak Frequency of Behavioral Symptoms with Progression of AD

Symptomatic domains over time

Most common/most distressing symptoms.

- Psychological
  - Delusions
  - Hallucinations
  - Depressed mood
  - Sleeplessness
  - Anxiety

- Behavioural
  - Pacing
  - Physical aggression
  - Wandering
  - Restlessness
Most persistent symptoms

- Wandering
- “Agitation” (restlessness, increased motor activity)
  – i.e., physical or verbal aggression

Symptoms that may respond to Rx

- Anxiety, restlessness, depressive symptoms.
- Withdrawal, apathy
- Elation, pressured speech and hyperactivity
- Delusions or auditory hallucinations
- Physical or verbal aggression
- Sexually inappropriate behaviour
Symptoms that do not tend to respond to Rx

- Simple wandering
- Inappropriate voiding
- Inappropriate dressing/undressing
- Perseveration
- Hiding, hoarding
- Eating inedibles

Therapy

- First think of the obvious:
  - Responsive behaviours:
    - i.e., Reversible causes
      - E.g., infection, cold, hot, hunger, recent change in routine &/or medications, etc
      - Appropriate pain management may be effective in reducing BPSD.
Nonpharmacologic Therapy

- Environmental modifications such as music, white noise, plants, animals
- Speak slowly, keep commands simple and positive, use gestures, gentle touch
- Behavioral management techniques
- Structured activities and use of schedules
- Massage, exercise

When to treat with medications?

- Personal biases, thresholds..
- Perceived CG stress
- Regulations
- Etc…
Pharmacotherapeutic principles for BPSD:

- Look for **symptom complexes** to help guide initial choice of agent.
  - E.g., depression, depression/anxiety, psychosis.

- Medications should be given in **lower doses** than recommended adults (50% less) and follow guidance from appropriate study data.

- Ideally, use agents with **demonstrable efficacy** as first line agents.
  - NB: Demonstrable does not = Health Canada or FDA approval….

- Carefully consider **side effects**……

**Associations between antipsychotics and adverse outcomes: The tale of safety.**
CVAE warnings for atypical antipsychotics

- Risperidone 2002-03
- Olanzapine 9/04
- Aripiprazole 1/05

“Black Box” warnings

- April 2005, FDA
- June 2005, Health Canada
- June 2008, FDA for typical APs
Bottom line?

- They are all potentially risky with a 1.5 to 1.8X greater risk of mortality.

Safety Considerations of particular importance in older people

- ↑ risk for antipsychotic-related AEs
  - EPS
  - Tardive dyskinesia (TD)
- Orthostatic hypotension
- Sedation
- Anticholinergic effects
- Cognitive impairment
- Cardiac conduction abnormalities
- ↑ fall risk due to any/all of above
### ANTIPSYCHOTIC SIDE EFFECTS

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**Evidence for the Efficacy of Antipsychotics and current use**

- The best of a bad bunch.....
Current evidence supports use of risperidone or aripiprazole, at least for up to 12 weeks for aggression or psychosis.

Efficacy and Adverse Effects of Atypical Antipsychotics for Dementia: Meta-analysis of Randomized, Placebo-Controlled Trials

Lou S. Schneider, M.D., M.S., Karen Dagerman, M.S., Philip S. Insel, M.S.

Risperidone; increased risk for death overall was reported elsewhere. Conclusions: Small statistical effect sizes on symptom rating scales support the evidence for the efficacy of aripiprazole and risperidone. Incomplete reporting restricts estimates of response rates and clinical significance. Dropouts and adverse events further limit effectiveness. Atypicals should be considered within the context of medical need and the efficacy and safety of alternatives. Individual patient meta-analyses are needed to better assess clinical significance and effectiveness. (Am J Geriatr Psychiatry 2006; 14:191-210)

The reality

- Risperidone or aripiprazole are not always effective (nothing is) nor always tolerated.

- Above factors (& others) lead to use of various drugs.

- Must therefore carefully consider evidence & be knowledgeable regarding alternatives and their safety profile in this vulnerable population....
Additional considerations

- Effect size for BPSD vs other diagnoses.
- Effect size for NH vs community subjects.
- Waxing and waning of BPSD/reassessment and discontinuation (to be covered later).

Are antidepressants helpful?

![Figure 1. Change in Neurobehavioral Factor Scores From Baseline to Study Termination (≤17 Days) in Patients With Dementia in a Randomized, Double-Blind, Placebo-Controlled Trial of Citalopram and Perphenazine](image)

- Significant difference within group between baseline and termination scores (Wilcoxon signed-rank test, *p* < 0.05).
- Significant difference between the citalopram and placebo groups (Kruskal-Wallis test, *p* < 0.05).
Are antidepressants helpful?


Before you say no, consider:
1. Study setting
2. Other benefits
3. Power
4. Severity of depression
5. 50% overall failure of antidepressant studies, and not many have been done in AD
6. Lack of response to one SSRI does not predict it to the other

These drugs are used empirically for depression & aggression.

5-HT drugs

- Fluoxetine: t ½ can be a problem.
- Fluvoxamine: Nausea can be a problem.
- Paroxetine: Anticholinergic properties.
- Citalopram/escitalopram: Very well tolerated.
  - Citalopram: 5-10mg/day, can increase to 20mg/day
  - Escitalopram: 5-10mg/day, may increase to 20mg/day
5-HT drugs

• Sertraline: Well tolerated, good second choice.
  – 25mg daily, may increase if needed.

• Trazodone: Very well suited for sleep and aggression.
  – Start with 25-50mg and titrate as needed

Mood stabilisers??

• VPA (Depakote and others)
  – Data from case reports & small case series.
  – Cochrane review concluded no benefit.
  – Dose to response/side effects.
  – Would you draw levels?

• Gabapentin
  – From case reports
  – Dose to response/side effects.
  – Drowsiness may be problematic
  – 100% renally excreted...
  – Best avoided
Mood stabilisers

- Carbamazepine
  - Evidence for efficacy better than with other mood stabilisers.
  - Can be difficult to use.
  - Would you draw levels?
  - Dosing?

Apathy Pharmacotherapy

- Evidence to guide us is scant...
  - AChEIs (donepezil)
  - Bupropion
  - Methylphenidate
  - ? Memantine
Inappropriate sexual behaviours

• Pharmacological approaches:
  – Eliminate drugs that are disinhibiting (etoh, BZPs)
  – Perhaps AChEIs
  – Most data are case reports
    • Citalopram, trazodone, quetiapine
    • Gabapentin
    • Estrogens
    • Leuprolide, cyproterone

Circadian Rhythm Disturbances

• Nonpharmacologic therapies include:
  – keeping patients awake during the day with various external stimuli
  – sometimes structuring short nap after lunch to avoid sundowning
  – early evening activities
  – stimulus control at night
  – “white noise”
  – bright light exposure
Circadian Rhythm Disturbances

- Pharmacologic interventions include melatonin, nonbenzodiazepine hypnotics (e.g. zopiclone, **trazodone**).

- Caregiver interventions include: educational programs, respite, and assistance with their own sleep needs.
Measuring effectiveness

• Keep it simple & look at/measure:
  – Frequency
  – Severity
  – XS work due to symptom

• Alternatively:
  – Goal setting?

How long to treat?

• Guidelines suggest attempt at lowering dose and stopping the medication after 3 months of stability.
  – E.g., Paranoid delusions or hallucinations occurred at ¾ consecutive visits over 2 years of f/u in only 10-15% of patients. (Devanand 1997)
Symptomatic domains over time

Discontinuing antipsychotics is NOT a new concept!

A RANDOMIZED TRIAL OF A PROGRAM TO REDUCE THE USE OF PSYCHOACTIVE DRUGS IN NURSING HOMES

Conclusions. An educational program targeted to physicians, nurses, and aides can reduce the use of psychoactive drugs in nursing homes without adversely affecting the overall behavior and level of functioning of the residents. (N Engl J Med 1992;327:168-73.)
Withdrawal of haloperidol, thioridazine & lorazepam in NH Residents

- DB controlled crossover trial: 60% completed
- Mean duration of therapy: 16.5 months
- No behavioral or functional differences detected after placebo crossover


Conclusions

For most patients with AD, withdrawal of neuroleptics had no overall detrimental effect on functional and cognitive status. Neuroleptics may have some value in the maintenance treatment of more severe neuropsychiatric symptoms, but this benefit must be weighed against the side effects of therapy.

Trial registration: Cochrane Central Registry of Controlled Trials/National Research Register (#ISRCTN33368770).
Summary

• Pharmacologic treatment is often indicated for BPSD.

• Use a structured approach (vs. using antipsychotics for all BPSDs).

• Revisit in a few months with a goal of stopping medications.
Web resources

- www.ipa-online.org
- http://livingwithdementia.uwaterloo.ca/
- www.alzforum.org
- http://www.alzheimer.ca/

Case 1

- 85 year old female with AD has recently been telling her CG that she enjoys having a doorman at their house everyday.
- CG tells you no such person exists and wonders what he should do.
- Standard workup is unremarkable.
- No new medications added or deleted.
- No other consequences noted.
Case 1

Which is the best treatment option?
A: Cholinesterase inhibitor
B: Trazodone
C: No drug therapy
D: Risperidone

Case 2

• 80 year old female with multiple diseases and medications
• Dx: AF, hypothyroid, OA, OP, HTN, atonic bladder
• Rx: include warfarin, APAP, thyroxine, etc
• Recent INR: 1.1; TSH: 18; BP: 175/86
Case 2

- CG reports patient only takes ~ 50% of her doses & has hit him and their daughter when they try and help with her medicines.
- She is also very angry, and believes her husband is having an affair.
- Also believes that he and their daughter are plotting to poison her with all these drugs.

Which is the best treatment option?
A: Cholinesterase inhibitor
B: Trazodone
C: Risperidone or aripiprazole
D: Olanzapine
Case 3

- 82 year old male with AD living in NH has been resisting care (i.e., bathing and grooming) & constantly gets up at night and wanders.
- The patient states he doesn’t care to be bathed four times a week and doesn’t like his new caregiver, Mike who works 3 days/week.
- Staff are able to provide care but they state that it takes longer on the days that Mike works.

Which is best treatment option?
A: Cholinesterase inhibitor
B: Trazodone
C: Valproic acid
D: No drug therapy
Questions?

We encourage you to report medication incidents

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<thead>
<tr>
<th>Reporting and Prevention Systems</th>
<th>Practitioners</th>
<th>General Points</th>
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<tbody>
<tr>
<td>REPORT a Medication Incident</td>
<td>Healthcare Professional (e.g., nurse, pharmacist, physician)</td>
<td>Preventing harm from medication incidents is not just a responsibility for health professionals - consumers too can play a vital role.</td>
</tr>
<tr>
<td>SafeMedicationUse.ca</td>
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<tr>
<td>CPNR - Community Pharmacy Incident Reporting Program</td>
<td>For participating community pharmacies.</td>
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<td>Analyze-ERR</td>
<td>For participating healthcare facilities.</td>
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Post-session Questionnaires:

- Post-session attendance statistics survey
- An Evaluation link will be sent to you
  - Please complete

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