Optimal Management of Challenging Behaviours in Dementia: An Update on Pharmacologic and Non-Pharmacologic Approaches

Andrea Iaboni, MD, DPhil, FRCPC

Toronto Rehab Institute, UHN
Learning objectives

• Recognize the expected benefits and side effects of medications used to manage challenging behaviours

• Construct a treatment plan for the management of challenging behaviours that incorporates recent evidence

• Consider a range of non-pharmacological behaviour management tools in a treatment plan
Outline

1. Review of challenging behaviours
2. Evidence-based recommendations about medications for challenging behaviours
3. From research to clinical practice:
   – Understanding clinical trials
   – Applying evidence to clinical practice
4. An approach to treating challenging behaviours in severe dementia
Definitions

Challenging behaviours

• Actions or activities that cause difficulty for the person or others
  – Aggressive and non-aggressive

Neuropsychiatric symptoms

• Psychiatric manifestations of disorders
Challenging behaviours

- Screaming
- Repetitive questions
- Constant requests for help
- Pacing
- Shadowing
- Undressing
- Masturbating publicly
- Inappropriate urinating
- Hoarding
- Dismantling
- Hiding items
- Intentional falling
- Eating/Drinking excessively
- Eating inappropriate substances
- Threatening
- Swearing
- Verbal abuse
- Hitting
- Pushing
- Spitting
- Biting
- Grabbing
- Pinching
- Scratching
- Hair-pulling
Neuropsychiatric Symptoms in Alzheimer’s Dementia

Lyketsos, JAMA, 2002
Current CCCDTD4 recommendations

- Medications if inadequate response to non-pharm interventions
- If evidence of depression consider antidepressants
- Risperidone, olanzapine, aripiprazole for severe agitation/aggression/psychosis with risk to self or others
- Limited evidence for antidepressants for psychosis/agitation
- Limited to no evidence for cholinesterase inhibitors, memantine, valproate, trazodone, quetiapine
UNDERSTANDING CLINICAL TRIALS
How do we study the effects of medications?

- Randomized controlled trials
- Short duration, small numbers
- Selection of subjects
- Heterogenous study population
  - Aggression/Agitation/Psychosis
- Dosing strategies fixed
- Clinically meaningful outcomes
- Placebo response
## Evidence for antipsychotic medications: CATIE-AD trial

<table>
<thead>
<tr>
<th></th>
<th>OLANZAPINE</th>
<th>RISPERIDONE</th>
<th>QUETIAPINE</th>
<th>PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean dose</td>
<td>5.5 mg</td>
<td>1.0 mg</td>
<td>56.5 mg</td>
<td></td>
</tr>
<tr>
<td>Discontinuation due to intolerance</td>
<td>24%</td>
<td>18%</td>
<td>16%</td>
<td>5%</td>
</tr>
<tr>
<td>Response (At least minimal improvement)</td>
<td>32%</td>
<td>29%</td>
<td>26%</td>
<td>21%</td>
</tr>
</tbody>
</table>

Schneider, 2006, NEJM
Cohen-Mansfield Agitation Inventory

• 29 different behaviours

• Scored by frequency:
  – 1 – Never, 2 - Less than once a week, 3 - Once or twice a week, 4 - Several times a week, 5 - Once or twice a day, 6 - Several times a day, 7 - Several times an hour

• 3 factors
  – Factor 1 - Aggressive behavior
  – Factor 2 - Physically nonaggressive behavior
  – Factor 3 - Verbally agitated behavior
Risperidone

- Meta-analysis of 3 trials
- Psychosis, Aggression, or Agitation (CMAI=60)
- N=809 people
- 10-13 weeks of treatment
- Compared with placebo

Schenider, 2006, AJGP
SSRI Antidepressant

- Meta-analysis of 2 trials
- Compared with placebo
- Agitation/Aggression, baseline CMAI=35
- N=250

Seitz, 2011, Cochrane review
Cholinesterase inhibitors and Memantine

• Studies often excluded people with behaviours

• 2 studies for Chel and 1 for memantine looking at acute agitation (baseline CMAI mid-60s) were negative

• Use in early dementia may delay or prevent onset of behavioural disturbances

• Side effects/ tolerability issues for Chel
Mean Total Scores on CMAI from Trial Entry through Follow-up for Treatment and Placebo Groups

Howard RJ, 2007, NEJM
Memantine

CMAI -2 weeks (screening) 0, 2, 4, 6, and 12 weeks

Fox, 2012, PLoS ONE
Benefits of medications

• Many challenges to assessing benefits of medications from clinical trials
  – Symptoms too variable, or too ill-defined (ie “agitation”) and difficult to measure change

• On aggregate, medications help about 30% of patients, with an average improvement by 2 points on behavioural scales above placebo
  – They help a few a lot, some a little, most not at all
Risks of medications

• Decision to use medications need to be put in context of risks
• Risks of medications are worrisome, but behaviours are also risky and distressing
• Risks always outweigh benefits where:
  – Expected benefits very minimal
  – Side effects of medication are very distressing or uncomfortable to patient
## Medication risks

<table>
<thead>
<tr>
<th>Antipsychotics</th>
<th>(in dementia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of parkinsonism</td>
<td>12%</td>
</tr>
<tr>
<td>Risk of tardive dyskinesia</td>
<td>5% per year</td>
</tr>
<tr>
<td>Risk of death</td>
<td>1.5x (3.5% vs. 2.3%; 1 death per 100 treated)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antidepressants</th>
<th>(in depressed elderly)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of falls</td>
<td>1.8 x</td>
</tr>
<tr>
<td>Risk of fractures</td>
<td>1.5 x</td>
</tr>
<tr>
<td>Risk of death</td>
<td>?</td>
</tr>
</tbody>
</table>
Antipsychotic-induced Movement disorders

- Dystonia
- Akathisia
- Parkinsonism
- Tardive dyskinesia
  - tongue protrusion
  - grimacing
  - rapid eye blinking
  - lip smacking, pursing, or puckering
  - other writhing involuntary movements
Guess the treatment “X”

- Moderate behavioural disturbance (excluding severely aggressive patients)
- N=352, baseline CMAI=49
Stepwise protocol for treatment of pain

- Individual approach based on current medication regime
- Acetaminophen oral (max. increase to 3 g/day),
- Extended release morphine oral (max. 20 mg/day), or
- Pregabaline oral (max. 300 mg/day)
- Buprenorphine transdermal plaster (if can’t swallow)
- Combinations if needed

Husebo, 2013, AJGP
Non-pharmacological interventions

Studies limited by small size, differing techniques and outcomes and rarely replicated

- Simulated presence or recorded conversation (Camberg et al., 1999; Garland et al., 2007)
- Aromatherapy with lavender (Holmes et al., 2002; Lin et al., 2007) or lemon balm (Ballard et al., 2002)
- Music therapies (Garland et al., 2007; Svansdottir and Snaedal, 2006).
Guess the Intervention

- N=72, mean CMAI = 61
- Clustering by nursing home
- Improvement in CMAI by 35% in treatment group and 11% in placebo

CHANGE IN CMAI SCORE

Intervention BETTER

Ballard, 2002, J Clin Psychiatry
Guess the intervention part 2

- N=289 nursing home residents
- Persistent need-driven behaviours making it difficult for staff to provide them with quality care
- Baseline CMAI = 50
CADRES: Person-Centred Care

- Included use of medications
- Improvement in behaviours
- More falls, more antipsychotic use (although drop from baseline)

Chenoweth, 2009, Lancet Neurol
AN APPROACH TO CHALLENGING BEHAVIOURS

N=1
Applying evidence to the individual: N=1

- OBSERVE AND MEASURE
- Non-pharmacological, person-centred interventions
- Careful selection of medication
- Start low, go slow
- OBSERVE AND MEASURE SOME MORE!
- Monitor for efficacy
- Monitor for side effects
- Plan for discontinuation
Red flags

• Targeted violence or threats of violence

• Aggression (as opposed to resistance)
  – Resistance = A defensive action, an attempt to protect the self from harm
  – Aggression = An offensive action, angry and destructive, intended to cause injury

• Behaviours based on complex delusional beliefs or hallucinations
  – Delusions vs Disorientation
Observe/Study/Discuss/Describe/Measure/Evaluate

- Not all agitation is alike!
- What are the symptoms underlying these behaviours?
- What are these behaviours communicating?
- Is there a pattern to the behaviour?
- Observe ourselves too: How are we managing the behaviour now? Can we be reinforcing the behaviour?
Challenging behaviour

Psychosis
Activity/Drive
Mood

Personal
Social
Environment
Non-pharmacological interventions

- Try them out!
- Be systematic—use a care plan, monitor adherence to the care plan and evaluate regularly.
- Involve families, the patient, all care staff
Symptom-based approach

Psychosis
- MILD: SSRI, ChEI
- MODERATE/SEVERE: Risperidone (Olanzapine), Aripiprazole

Activity/Drive
- No evidence

Mood
- Pain management: SSRI
Use of medications

- Start low, go slow but keep going if tolerated, have target in mind

<table>
<thead>
<tr>
<th>For behaviours in dementia</th>
<th>Initial dose</th>
<th>Target dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>0.125mg</td>
<td>0.5-1mg</td>
<td>2mg</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>2mg</td>
<td>5-10mg</td>
<td>15mg</td>
</tr>
<tr>
<td>Sertraline</td>
<td>25mg</td>
<td>100-150mg</td>
<td>200mg</td>
</tr>
<tr>
<td>Citalopram</td>
<td>5mg</td>
<td>10-20mg</td>
<td>30-40mg *monitor QTc</td>
</tr>
</tbody>
</table>
Monitor for efficacy

1) Observe and re-measure!
2) Have realistic treatment expectations
3) If no benefit or worsening, re-consider the treatment (change dose, change agent)
4) Don’t persist with something that hasn’t been helpful!
Monitor for side effects

- Parkinsonism
- Tardive Dyskinesia
- Akathisia
- Falls
- Worsening confusion
- Hyponatremia with SSRI antidepressants
- Cardiac side effects
Plan for trial discontinuation

• Early (within 3-4 months) discontinuation of antipsychotics is now seen as standard of practice

• Several discontinuation trials to date showing little symptom exacerbation (for most patients)
  – ADAD: 60% switched to placebo were relapse-free at 32 weeks
  – Baseline severity of behaviour is risk factor for relapse

Devanand (2012) NEJM
N=1 in practice

- Observe/Measure: ABC charting, behavioural logs, behavioural scale
- Formulation of behaviour, underlying symptoms and causes
- Systematic application of non-pharm interventions (care plan with monitoring)
- Initiate medications: slow but steady
- Observe/Measure: Benefits and side effects
Conclusion

• Clinical trials demonstrate some benefit for medications for challenging behaviours in dementia, but also illustrate their limitations.

• Non-pharmacological approaches are also effective with few down-sides.

• Optimal treatment for challenging behaviours is INDIVIDUALIZED and SYSTEMATIC.