PROMOTING MORE EFFECTIVE MEDICATION USE BY SENIORS

# DUE Quarterly

Issue 47 DRUG USE IN THE ELDERLY July 2005

# Treatment considerations to manage dementia

Approximately 350,000 Canadians have dementia, estimated to increase to 750,000 by 2030; 8% are older than 65 years, 40% older than 85.

Behavioral and psychological symptoms of dementia (BPSD) are an integral part of the clinical spectrum of the illness, affecting up to 90% of patients.

BPSD is defined by the International Psychogeriatrics Association (IPA) as "symptoms of disturbed perception, thought content, mood and behavior."

## BPSD considerations

- ★ BPSD is associated with rapid cognitive decline, decreased quality of life, high utilization of pharmacotherapy, use of physical restraints, high caregiver distress and increasing financial costs. But effective intervention and treatment can reduce patient and caregiver distress, improve quality of life and delay negative outcomes.
- ★ BPSD symptom clusters include aggression, agitation, apathy, depression and psychosis.
- ★ BPSD, particularly depressive symptoms, can precede diagnosis up to three years and become more prevalent as the disease progresses. BPSD symptoms can worsen and recur, but 45% of patients experience resolution.

## Agitation

- ★ Cohen-Mansfield definition: Inappropriate verbal, vocal or motor activity not explained by medical condition, social/ environmental disruption, apparent unmet needs or confusion.
- ★ Involves excessive non-productive motor activity and unpleasant emotional tension/distress.

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- ★ Cohen-Mansfield Agitation Inventory (CMAI) subtypes:
  - Physically aggressive – hitting, scratching, kicking, pushing
  - Physically non-aggressive – restless, pacing, wandering
  - Verbally aggressive – screaming, cursing
  - Verbally non-aggressive – negativism, attention seeking (importuning), complaining, whining

## Etiological correlates of BPSD

Etiological correlates are usually multifactorial with underlying psychological, medical, environmental and social concomitants. For example:

- ★ Severity and nature of cognitive impairment
- ★ Premorbid or changes in personality during dementia
- ★ Language impairment
- ★ Sensory deprivation – auditory and visual
- ★ Medical comorbidity, physical discomfort, predisposed to delirium
- ★ Brain degeneration – frontal and temporal lobes
- ★ Neurotransmitter changes – cholinergic, hypothalamic, serotonergic and noradrenergic dysfunction
- ★ Circadian rhythm changes – "sundowning"
- ★ Environmental factors – physical surroundings, ambience (noise, climate, darkness), caregiver and co-resident attitudes

### Next issue . . .

- Drugs that impact seniors' nutritional intake

*DUE Quarterly offers expert opinions – not ACP-AMA guidelines or evaluations of drug use.*

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*Together, the physician, pharmacist and patient can all make a difference!*

## Clinical assessment and management

- ★ A systematic clinical approach, involving family and team, ensures safety of patient, caregivers and other residents.
- ★ Identify and describe target behaviors with context, precipitants (antecedents) and consequences. Use ABC model, i.e., identify trigger, describe behaviors and result of behavior (e.g., excessive social stimulation precedes aggressive behaviors leading to altercation with family and/or co-residents).
- ★ Do a physical examination and medical assessment to rule out concomitant medical illness (e.g., infection) and delirium.
- ★ Optimize management of chronic medical conditions and alleviate physical discomfort (specifically review pain management, bowel and bladder patterns, skin, hydration, nutrition, sensory impairments and removal of physical restraints).
- ★ Review concomitant medications with pharmacist, eliminate or minimize medication use that could contribute to confusion. Pharmacists should alert physicians to the patients' use of herbal or non-prescription products that could be contributing to confusion.
- ★ Consider non-pharmacological interventions (with limited evidence) including:
  - Social contact – one-to-one interaction, pet therapy
  - Sensory enhancement – massages, music, sensory stimulation, aromatherapy
  - Behavior therapy – differential reinforcement (e.g., reward quiet behavior, ignore outbursts, use distraction), stimulus control
  - Structured recreation and physical activities
  - Environmental adaptations – enhanced wandering areas to ensure safety, optimal levels of stimulation
- ★ Consider psychotropic medication as adjunctive treatment when behavioral/environmental interventions have failed or when associated with acute distress, danger to self or others, persistent symptoms, disruption of functioning or interference with ability to receive care.
- ★ Identify realistic goals of therapy to reduce targeted symptoms before initiating medication. Review regularly for efficacy and side-effects. Consider lowering dosage or discontinuing once behavioral stability is achieved.
- ★ Communicate clearly, among team members and with family, the expected outcome and potential risks.

## General pharmacotherapy principles and precautions

- ★ Mandate lower dosages; age-associated changes in pharmacokinetics and pharmacodynamics, comorbid medical illness and concomitant medication use render seniors more susceptible to adverse effects.
- ★ Balance expected benefits against potential risks/adverse events:
  - Excessive sedation, decreased cognition or increased confusion
  - Anticholinergic effects – dry mouth, blurred vision, aggravation of cardiac disease, constipation, urinary retention
  - Tardive dyskinesia (TD) – involuntary movements of lips, tongue and extremities
  - Extrapyramidal effects (EPS) – acute dystonia, parkinsonism or akathisia
  - Gait changes and increased risk of falling
  - Orthostatic hypotension
  - Neuroleptic malignant syndrome (NMS)
  - Serotonin syndrome
- ★ Match target psycho-behavioral cluster with the most appropriate medication class. Continue treatment for three-to-six months after positive response, then taper and trial discontinuation.
- ★ For acutely aggressive, agitated or psychotic behavior, use parenteral (IV/IM) medications.
- ★ Use rapid disintegration formulations (M-tabs, Zydis) for non-compliance with oral medications.

## Therapy goals

- ★ Relieve symptoms
- ★ Improve patient's quality of life
- ★ Reduce caregiver stress

## Pharmacotherapies

**None of the pharmacotherapies, except risperidone, have official Health Canada-approved indications for management of BPSD; their uses are considered off label.**

***Antipsychotics***

- ★ As an adjunct to non-pharmacological interventions
- ★ Best-studied pharmacotherapy
- ★ Consistent, but modest, beneficial effects in randomized controlled trial studies (RCTs)

***Typical antipsychotics (haloperidol, loxapine)***

- ★ Consider when atypical antipsychotics fail and in parenteral administration (PRN basis) in acutely agitated patients.
- ★ Less desirable in seniors for first-line maintenance treatment due to prominent side-effects of sedation, anticholinergic effects, EPS and TD.
- ★ Avoid in Lewy Body Dementia (LBD) and Parkinson patients (aggravate motor symptoms).

***Atypical antipsychotics (risperidone, olanzapine, quetiapine)***

- ★ June 2005 Health Canada advisory: Atypical antipsychotics in elderly patients with dementia in studies had a 1.6 fold increase in death rate, primarily from heart-related events or infections. Use cautiously after non-pharmacological measures.
- ★ American Expert Consensus Guidelines endorse use as first-line therapy for agitated dementia with delusion or second-line option for agitated dementia without delusion.
- ★ Clozapine not used in BPSD management due to significant risk of agranulocytosis.
- ★ Less EPS and TD reported, but associated with weight gain, cardiovascular effects (QT prolongation), cerebrovascular adverse events (CAEs) in patients with predisposing factors such as hypertension, atrial fibrillation and diabetes.
- ★ Consider regular periodic

*Continued on page 4 . . .*

# Practically speaking . . .

## Appropriate medication use for BPSD

### BPSD more likely to require/respond to medications

- Psychotic symptoms (most commonly persecutory delusions, visual hallucinations and less common auditory hallucinations, misidentification of self, others or events)
- Verbal aggression (moderate to severe and persistent)
- Physical aggression (moderate to severe and persistent)
- Interference with ability to receive care
- Dangerous to self
- Dangerous to others (co-patients, staff, family)
- Depression/apathy

### BPSD less likely to require/respond to medications

- Physical non-aggression: Motor restlessness, pacing, wandering, inappropriate dressing/ undressing, hiding/hoarding, willfulness
- Verbal non-aggression: Repetitive questioning, repetitive requests and gestures, screaming

(*Teri et al, 2000*)

### BPSD to warrant specialist referral

- Persistent and severe symptomatology in spite of thorough medical and environmental assessment and intervention
- Dangerous to self or others (co-patients, staff, family)
- Limited or no response to non-pharmacological approaches
- Limited or no response to medication use or evidence of adverse side-effects to medication use
- Inability to receive care despite non-pharmacological and pharmacological interventions

*– Compiled by Dr. William T. Chimich and Sandra Leung*

### Precipitants that may trigger BPSD

| | |
|---|---|
| Cognitive loss | • Extent of cognitive loss<br>• Hallucinations/delusions |
| Health changes | • Acute illness (infection, CHF)<br>• Pain<br>• Medication changes<br>• Constipation<br>• Fatigue |
| Caregiver behavior | • Changes in routines<br>• Caregiver approach |
| Environmental stimuli | • Overstimulation – lighting, noise levels, change in room (translocation), other residents (in communal settings) |
| Mood alteration | • Depression<br>• Changes within the family |
| Communication loss | • Progression of aphasia |
| Sensory changes | • Sensory deprivation – progression of hearing/visual loss |

*– Compiled by the DUE Quarterly Communications Advisory Committee*

*Continued from page 2 . . .*

monitoring of fasting blood sugar, A1C and lipid profile (three months after initiation of therapy and at six-month intervals after).

➢ ***Risperidone***

★ Recommended dose range: 0.25-2 mg/24 hours.

★ Largest and most definitive RCTs in dementia.

★ Only atypical agent with official indication in Canada for BPSD.

★ Risks at higher doses (i.e., more than 2 mg/24 hrs) for adverse effects: akathisia, hypotension, TD, sedation, edema.

★ Lowest reported rates of weight gain and metabolic syndrome compared to other atypical antipsychotics.

★ Temporal relation of CAEs but no established casual relationship. A 2003 study of 345 nursing home patients showed six CAEs in five patients with vascular or mixed dementia and one CAE with Alzheimer's disease (AD). All six patients had underlying cardiac and cerebrovascular disease risk factors.

➢ ***Olanzapine***

★ Dose range: 1.25-10 mg/24 hrs.

★ Low dose (5-10 mg/day) is superior to placebo in agitated dementia patients reducing emergence of psychosis.

★ IM formulation is as effective and safe as IM lorazepam.

★ Reported increased risk of CAEs compared to placebo especially in vascular or mixed dementia.

★ Adverse effects include sedation, liver enzyme elevation, antihistaminic effect and weight gain, EPS and TD risk, at higher doses.

➢ ***Quetiapine***

★ Dose range: 12.5-200 mg/24 hrs.

★ No RCTs published data.

★ Due to low risk of EPS and TD, consider first-line therapy for patients with LBD or with Parkinson's disease.

★ Adverse effects include sedation, hypotension, liver enzyme elevation and weight gain.

## Antidepressants

★ Citalopram and sertraline are the best-studied SSRIs.

★ Evidence that SSRIs are helpful in reducing symptoms of anxiety, agitation, aggression, irritability, depression and disinhibition.

★ No RCT evidence on use of novel antidepressants (venlafaxine, mirtazapine, bupropion). Anecdotal studies suggest SSRIs are useful for BPSD in frontal temporal dementia.

## Anticonvulsants

★ Largest RCT evidence after antipsychotics.

★ American Expert Consensus Guidelines suggest considering adding to atypical antipsychotic if required for agitation.

★ Carbamazepine has demonstrated limited benefit in RCTs. However, concerns for hepatic and hematologic toxicity and drug interactions limit use.

★ Valproic acid is perceived as a safer alternative, however, GI tolerability, sedation, gait ataxia, liver enzyme elevation and thrombocytopenia pose as significant risks.

★ Newer anticonvulsants (gabapentin, lamotrigine, topiramate) have limited or no RCT data in BPSD use.

## Anxiolytics

★ Antipsychotics and antidepressants may have anxiolytic effects in BPSD.

★ Short-acting benzodiazepines are limited to short-term and PRN use for specific circumstances (prior to care, medical procedure) due to concerns of adverse effects such as: excessive sedation, hypotension, falls, increased confusion and possible paradoxical agitation.

## Cholinesterase inhibitors

★ Donepezil, rivastigmine and galantamine are approved for treatment of mild-to-moderate AD. They have been shown to reduce the emergence of BPSD, reduce psychotropic drug use and delay institutionalization.

★ Some level 1 evidence in BPSD management associated with LBD showed improvement in neuropsychiatric domains of psychosis, apathy and aberrant motor behavior.

★ Adverse effects include nausea, vomiting, diarrhea, anorexia, bradycardia, bronchospasm.

## Others

★ Evidence-based data lacking for beta-blockers, anti-androgens for sexual aggression and ondansetron use.

★ Electroconvulsive therapy (ECT) may be used in severe vegetative depression in dementia with acute medical decompensation.

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**References available on request.** DQ

## We'd like your feedback . . .

***DUE Quarterly*** **focuses on the provision of practical drug management information for practising clinicians. Your comments and suggestions for future articles are welcome. Please contact:**

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