Management of behavioural and psychological symptoms of dementia

With the steady rise in numbers of the world's elderly population, the behavioural and psychological symptoms of dementia (BPSD) have become increasingly relevant to both clinicians and families.

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Approximately 35 million people worldwide have dementia and this number is predicted to increase to 115 million by 2050.[1] Behavioural and psychological symptoms of dementia (BPSD) are a common complication of dementia and between 70% and 90% of people with dementia will experience BPSD at some point during their illness. BPSD results in significantly greater caregiver burden, higher health-related economic costs, poor quality of life and premature placement in nursing homes.[2] The presence of BPSD has also been associated with disease progression and greater cognitive decline in Alzheimer's dementia (AD).[3] Recognition of BPSD by the healthcare provider forms a central component of the management of patients with dementia syndromes. This article aims to provide clinicians with an overview of BPSD and an approach to management, incorporating both non-pharmacological and pharmacological strategies.

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Behavioural and psychological symptoms of dementia

Cognitive impairment is a central feature of dementia. However, multiple brain processes are disrupted as part of the disorder, leading to a range of neuropsychiatric symptoms. Neuropsychiatric symptoms in people living with dementia are often referred to as BPSD, as they incorporate symptoms of disturbed perception, thought content, mood or behaviour.[4] These symptoms are listed in Table 1.

Patients may experience varying symptoms, or combinations thereof, depending on the underlying cause or stage of illness. Patients with more severe dementia (roughly correlating with lower Mini Mental State Exam (MMSE) scores) are at increased risk for psychosis, agitation and behavioural disturbance.[5] The type of symptom may also assist with the diagnosis, e.g. visual hallucinations are frequently seen in Lewy Body dementia.

Aetiology of BPSD

By definition, BPSD occurs in the context of dementia, and may be the direct result of the disorder, or aggravated by additional factors. These include biological (e.g. pain, systemic infection, dehydration, electrolyte disturbance, constipation), psychological (e.g. exaggeration of pre-morbid personality traits, grief due to multiple losses, depression) and environmental (e.g. change of caregiver) components. Language impairment and disrupted thought processes may render the patient unable to communicate the cause of their distress, subsequently leading to behavioural disturbance.

When making the diagnosis of BPSD, limitations in communication with the patient result in clinicians relying heavily on reports from family members and caregivers.

Making a diagnosis of BPSD

Clinicians managing patients with BPSD should seek to confirm the type and severity of dementia present. This will include collateral, bedside cognitive evaluation and appropriate special investigations. When making the diagnosis of BPSD, limitations in communication with the patient result in clinicians relying heavily on reports from family members and caregivers. Clinical syndromes that do not result in gross behavioural disturbance, e.g. depression, are frequently under-reported, leading to under-diagnosis and a missed opportunity for treatment. A number of clinical measures, specific to dementia, have been designed to aid in the diagnosis of BPSD. These measures provide a useful guide to a range of potential BPSD, their severity, impact

Table1. List of BPSD

Behavioural		Psychological/psychiatric	
Physically non-aggressive	Agitation Pacing Inappropriate object handling Wandering Shadowing Restlessness Negativism Hoarding	Mood disturbance	Depression Suicidal ideation Irritability Anger Emotional lability Inappropriate jocularity/laughter Euphoria
Physically aggressive	Hitting Kicking Biting	Anxiety	Anticipation anxiety Panic symptoms Generalised anxiety
Verbally non-aggressive	Repetition of sentences or requests Complaining Repetitive singing	Apathy	Decreased motivation Social withdrawal Emotional indifference Diminished reactivity Avolition
Verbally aggressive	Screaming Swearing	Psychosis	Delusions Misidentification syndromes Hallucinations (auditory,visual)
		Personality change	Disinhibition Blunting Exaggeration of pre-morbid traits

on caregivers, and allow the clinician to monitor treatment efficacy in collaboration with the patient's family. These measures include: the neuropsychiatric inventory; the behavioural pathology in Alzheimer's disease rating scale; Cornell scale for depression and the Cohen-Mansfield agitation inventory.[6-9] Families should be encouraged to record a 24-hour behaviour chart over a few days to identify potential precipitants or problematic time periods, e.g. bath time. Once a diagnosis has been made, the target symptom, its duration, possible underlying cause and treatment strategy should be communicated to the patient and caregiver.

Management of BPSD

Paramount to the management of BPSD is the recognition of any underlying contributing physical illness (such as delirium), psychological issues or environmental change. Features suggestive of delirium include acute onset, confusion, fluctuation of mental state, sun-downing and evidence of a systemic disturbance. Drug-induced delirium, e.g. anticholinergics, antihypertensives and antipsychotics, should always be considered in the differential diagnosis and management of BPSD.

Few longitudinal studies of BPSD exist. Some studies suggest that many symptoms remit spontaneously after a few months. However, agitation, aggression, severe depression and psychosis are less likely to resolve without treatment and require active management.[10]

Table 2. Non-pharmacological management strategies

General principles
- Provide a 'dementia-safe' and friendly environment
- Maintain a set routine
- Avoid over-stimulation
- Psychoeducation for family/caregivers
- Adequate training for caregivers
- Reminders and repetition of information
- Orientation with clocks, calendars, newspapers
- Regular social interaction and activity

Behavioural
- Regular exercise
- Wandering paths (secure)

Psychosocial interventions
- Reminiscence therapy
- Validation therapy
- Resolution therapy
- Pet therapy
- Respite care to relieve caregiver burden
- Supportive counselling for family members, e.g. dementia support groups

Non-pharmacological management strategies

Non-pharmacological management is considered first line in the management of BPSD and should be employed regardless

of whether a decision is taken to commence medication. Routine monitoring and evaluation need to be undertaken on a regular basis by the clinician. These strategies are listed in Table 2.

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Table 3. Principles of prescribing in BPSD

- Always use the lowest efficacious dose
- Titrate slowly
- Monotherapy if possible
- Consider drug-drug interactions
- Withdraw drug if no benefit, and prior to commencing another agent
- Full disclosure of risk v. benefit to patient and family

Pharmacological treatment of BPSD

A modest number of individuals with dementia may require pharmacotherapy for the treatment of BPSD. Antipsychotics have traditionally been the treatment of choice for the management of behavioural disturbance in dementia. Due to the recent Food and Drug Administration (FDA) warnings of the increased risk of stroke in elderly patients using all classes of antipsychotics and risk of worsening confusion in dementia, these drugs are now considered second line.[11] A useful approach when deciding on an appropriate agent would be to first identify and treat depression and anxiety disorders if present, secondly to consider cognitive enhancers where appropriate, and finally consider alternative agents, e.g. anticonvulsants and antipsychotics. When prescribing, consider the principles listed in Table 3.

The remainder of this article focuses on specific BPSD syndromes with treatment options. Table 4 provides recommended treatment doses.

Depression

Untreated depression increases mortality, exacerbates cognitive and functional decline, impairs quality of life and increases caregiver burden. Between 30% and 50% of patients with dementia have depressive symptoms. Selective serotonin reuptake inhibitors (SSRIs), e.g. citalopram and sertraline, are widely available and are favoured as the treatment of choice in dementia with co-morbid depression. Tricyclic antidepressants (TCAs), e.g. amitriptyline, may be considered as second line, although the anticholinergic, antihistaminic and cardiotoxic side-effects are problematic in this population.[12] Treatment response may be longer than that seen in adult populations.

Anxiety

Anxiety symptoms, e.g. anticipatory anxiety, may be disabling and place additional strain on caregivers. Anxiety symptoms are prominent in vascular dementia, frontotemporal dementia, and dementia associated with Parkinson's disease, when compared with Alzheimer's disease. A high co-morbidity exists between anxiety and depression and both conditions should be addressed. Limited guidelines exist for the treatment of anxiety in dementia. However, most clinicians recommend

Table 4. Recommended doses in elderly patients

Medication		Additional notes
Antidepressants		
SSRIs	Citalopram 20 mg/day: initiate at 10 mg	Few CYP450 interactions
	Fluoxetine 20 - 40 mg/day	Inhibits CYP450 2D6 & 3A4
	Sertraline 50 - 100 mg	Some dopaminergic activity
TCAs	Amitriptyline initial dose 25 - 50 mg/day, increase gradually to 100 mg/day	Cardiotoxic, anticholinergic, antihistaminic side-effects Hypotension
SARI (serotonin 2 antagonist/ reuptake inhibitor)	Trazodone 25 mg at night	Antihistaminic side-effects Hypotension
Cholinesterase inhibitors	Donepezil 5 - 10 mg at night	GIT side-effects are common in all three
	Galantamine 16 - 24 mg/day	
	Rivastigmine 6 - 12 mg in 2 doses	
NMDA receptor antagonist	Memantine 10 mg twice daily	Dizziness and headache may occur
Anticonvulsants	Sodium valproate 10 -15 mg/kg in divided doses	Start with smaller dose and titrate up
	Carbamazepine 400 mg/day in divided doses	CYP450 3A4 inducer
Antipsychotics		
Typical	Haloperidol 0.5 - 1 mg/day	Watch for EPSEs
Atypical	Risperidone 0.5 mg twice daily: may initiate at 0.25 mg twice daily	Weight gain, may increase prolactin
	Quetiapine 25 - 50 mg at night	Hypotension, sedation, weight gain
	Olanzapine 2.5 - 10 mg/day	Weight gain

the use of antidepressants to treat anxiety symptoms. Benzodiazepines are relatively contraindicated due to their cognitive side-effects, risk of respiratory depression in elderly patients with chronic obstructive airway disease (COAD), increased risk of falls and capacity for physical dependence.[13]

Non-pharmacological management is considered first line in the management of BPSD and should be employed regardless of whether a decision is taken to commence medication.

Psychosis

Antipsychotics are indicated for the treatment of intrusive delusions and hallucinations associated with dementia. Each antipsychotic confers its own risk versus benefit profile and the choice of agent should be made according to the needs of the individual patient. Typical, or first-generation antipsychotics (FGAs), increase the risk of developing extra-pyramidal side-effects (EPSEs), i.e. parkinsonism, acute dystonia, akathisia and tardive dyskinesia. Atypical, or second-generation antipsychotics (SGAs), may cause dyslipidaemias, impaired glucose tolerance and weight gain leading to a metabolic syndrome.[14] A risk-benefit analysis should be undertaken in every patient, taking into account both medical co-morbidities and propensity to develop disabling side-effects. Treatment is not recommended for periods longer than 3 months. However, in more severe cases treatment may be required for a longer duration.

Sleep disturbance

Sleep disturbance is common in dementia and may be associated with or form part of BPSD. Patients with AD may experience day-night reversal and those with Lewy Body dementia are at increased risk of REM sleep disorders. Co-morbid medical conditions, e.g. electrolyte disturbance, dehydration and infection, must be excluded as possible causative factors. Medications known to disrupt sleep should be evaluated.

Caregivers are often surprised when informed of the physiologically decreased need for sleep associated with normal ageing. Psycho-education forms part of management with regard to sleep hygiene and the importance of a daily routine. Naps during the day should be strongly discouraged. Some evidence exists for the use of antidepressants, e.g. SSRIs and trazodone, to address sleep disturbance in dementia. Non-benzodiazepine hypnotics, e.g. zolpidem, may be considered as a short-term measure. Tolerance and dependence may occur with these sedatives and caution is needed when co-prescribing additional central nervous system depressants. The use of benzodiazepines for sleep disturbance in dementia is not advised.

Agitation and aggression

Agitation and aggression form part of the BPSD spectrum and occur in up to 50% of patients with advanced dementia. No universally agreed upon definition for agitation exists and the term includes a range of problem behaviours from wandering to frank aggression. As mentioned previously, exclusion of an underlying medical cause, including delirium, is essential to management. Clinicians and family should adopt an empathic, non-punitive, person-centred approach to managing the behaviour. Non-pharmacological management strategies are a core component of treatment. A number of pharmacological options are available for cases of severe behavioural disturbance. These are discussed below.

In cases of mild to moderate AD, the cholinesterase inhibitors (CHEIs) have had some success in improving behaviour. Three agents – donepezil, galantamine and rivastigmine – are available. These agents have similar efficacy data although side-effects vary from person to person. A second agent should be attempted if the first is intolerable. Memantine is an *N*-methyl-D-aspartate (NMDA) receptor antagonist approved for moderate to severe AD. Positive behavioural change in cases of vascular dementia and AD have been reported.

Anticonvulsants, e.g. sodium valproate and carbamazepine, may be considered in severe cases of behavioural disturbance in all dementias. Drug-drug interactions between anticonvulsants (mostly metabolised by the liver) and concurrent medications may be problematic. As a second-line option, antipsychotics have a place in the management of severe agitation associated with dementia.[15] No antipsychotic is licensed for the treatment of dementia and is thus prescribed off-licence. Families should provide informed consent and referral to a psychiatrist is indicated in treatment-refractory cases.

Conclusion

The BPSD are common and cause significant distress among patients and caregivers. A number of effective non-pharmacological and pharmacological treatment options are available to clinicians in the management of BPSD.

Declarations of interest

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References available at www.cmej.org.za

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- BPSD affects between 70% and 90% of individuals with dementia.
- BPSD leads to increased caregiver burden, increased economic cost, decreased quality of life and premature placement in residential homes.
- The cause of BPSD is often multi-factorial.
- Behavioural disturbance may be an attempt to communicate distress.
- Delirium is the commonest cause of acute behavioural disturbance in dementia.
- Non-pharmacological treatment is considered first line in the management of BPSD and should be employed with or without drug therapy.
- Antipsychotic medications increase the risk of CVA and are considered second line in the treatment of BPSD.
- Depression affects between 30% and 50% of people with dementia and should be actively managed.
- Sleep disturbance may be caused by co-morbid medical conditions or certain medications.
- A full risk-benefit profile should be undertaken when prescribing anti-psychotics for BPSD.