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Therapeutic approaches in the management of behavioral and psychological symptoms of dementia in the elderly

A guideline produced by the Vancouver Coastal Health Authority describes how to assess patients in acute and residential care and identify the best nonpharmacological and pharmacological options for treating agitation, psychosis, and mood disorders.

ABSTRACT: More than 90% of patients with dementia will eventually develop behavioral and psychological symptoms of dementia, which include agitation, psychosis, and mood disorders. The Vancouver Coastal Health Authority has recently produced a guideline for the assessment, nonpharmacological treatment, and pharmacological treatment of aggression and agitation in patients with dementia in acute or residential care. The guideline reflects research that has found atypical antipsychotic agents to be effective for aggressive forms of behavioral and psychological symptoms of dementia. Pharmacological alternatives to atypical antipsychotic medications that have also been found to be effective include typical antipsychotic medication, cholinesterase inhibitors, antidepressants, and anticonvulsants.

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Dementia is a devastating illness for both patients and their families. A patient with dementia has memory loss and at least one other impairment: aphasia, apraxia, agnosia, or disturbance in executive functioning.[1] Of those patients with dementia, more than 90% will eventually develop behavioral and psychological symptoms of dementia (BPSD).[2] These include agitation, psychosis, and mood disorders.[3] After co-occurring medical conditions are ruled out, initial management of BPSD consists of nonpharmacological approaches, and then pharmacological ones when absolutely needed.

A guideline recently produced by the Vancouver Coastal Health Authority (VCH) helps clinicians tailor treatment specifically for the individual patient and weigh the benefit of an intervention carefully against the risk.[4] The VCH guideline was developed by geriatric psychiatrists and pharmacists within the region and is endorsed by the Regional Pharmacy and Therapeutics Committee, the Health Authority Medical Advisory Council, and the VCH Professional Practice Directors. The VCH guideline is intended to reflect evidence-based practice, but it should not be taken as absolute guidance in every situation. It may not be entirely appropriate in a different setting or health authority, and may be subject to revision.The biopsychosocial approach recommended when managing BPSD requires investigating medically reversible symptoms before initiating atypical antipsychotic therapy.

Behavioral and psychological symptoms of dementia

Agitation, psychosis, and mood disorders are the core concerns for clini-

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cians managing patients with BPSD. Depression occurs in 20% of patients with Alzheimer disease[5] and is more frequent and persistent in those with vascular dementia.[6] Psychosis in the form of hallucinations and delusions occurs in 25% of patients with dementia.[3] Delusions are usually non-bizarre and often persecutory regarding theft.[7] Agitation occurs in 20% of outpatients[8] and 40% to 60% of inpatients, including those in residential care settings.[9] Agitation can be aggressive and involve restlessness/pacing, verbal insults, shouting and physical aggression,[5] or nonaggressive and involve wandering, exit-seeking behavior, and disruptive vocalizations.[4] BPSD can be distressing to the patient and can increase caregiver burden and lead to earlier institutionalization.[10] A management strategy that begins with patient assessment and includes the carefully monitored use of atypical antipsychotic agents can offer some relief to patients and their caregivers.

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Assessment and tracking of BPSD

The first priority in assessment should be to ensure the safety of the patient and caregiver.[11] The symptoms and signs should be documented as described in the VCH guideline,[4] using an ABC approach that focuses on Antecedents, Behaviors, and Consequences.[11-13] Caregivers should note specifically what type of behavior (e.g., verbal, physical, sexual) results from what type of antecedent (e.g., morning care routine, meals, ambulation), or if the behavior is unprovoked.[11]

Standardized tools can be useful when tracking behaviors of patients with dementia. The Dementia Observation System is available online on the Canadian Academy of Geriatric Psychiatry's website http://bit.ly/WEj9WO. This chart could be completed on admission to a long-term care facility, or at any stable point in a patient's life. In addition, the patient's baseline alertness, cognitive function, and capacity to perform activities of daily living should be documented.[14] A tool such as the Behavioral Vital Signs chart[15] can be used to track symptoms and signs, and the patient's response to interventions over time. Caregivers can use the chart to report on agitation, delusions, hallucinations, depression/anxiety, manic states, sleep/wake cycle, and apathy over a 2-week period to provide the interdisciplinary care team with more information prior to the assessment.

The biopsychosocial model commonly used in psychiatry for understanding illness is useful for BPSD. Many biological factors can contribute to the development of dementia symptoms, including delirium, pain or discomfort, infection, metabolic issues, neuropsychiatric issues, polypharmacy, substance abuse or withdrawal, or dietary and drug interactions.[16] Every effort should be made to thoroughly investigate medically reversible causes of these symptoms to ensure the best treatment for the patient suffering with dementia. This may require ordering a panel of laboratory tests (CBC, electrolytes, urea, creatinine, phosphate, magnesium, calcium, albumin, liver profile, liver function, TSH, vitamin B12, PSA, urinalysis) and radiological investigations (CT head, KUB X-ray, chest X-ray, bone X-rays).

Psychosocial issues influencing the development of BPSD are also numerous.[11,13,17] Communication factors include problems with hearing or sight and language barriers. Examples of environmental factors are excessive or inadequate stimulation; unmet dietary needs or acknowledgment of preferences; and inappropriate room temperature, clothing, furniture, or medical equipment. Family factors include conflict, caregiver strain, financial concerns, and absence or loss of family supports. Addressing reversible factors is of paramount importance.

Nonpharmacological intervention

Despite evidence showing that physicians do not usually use nonpharmacological interventions first,[16] and that in an emergency situation pharmacological therapy may be needed, the general principle of investigating the

patient's symptoms thoroughly with a biopsychosocial approach still holds. A psychosocial care plan that emphasizes "interest, social activity, and comfort" should be created.[14] During treatment with pharmacological agents, the patient's circumstances should continue to be optimized.[14] A pharmacist should also be consulted to assess medication-related effects.[4]

The VCH guideline recommends that atypical antipsychotic medications be used when "there is a significant risk of harm to the patient or others, or when agitation or aggressive symptoms are persistent, recurrent, or severe enough to cause significant suffering and distress, or significant interference with care."

Given the complexity of the workup, the VCH guideline discourages telephone orders to initiate drug therapy. Instead, the guideline advises that a physical assessment of the patient be completed, and encourages the gathering of collateral information and laboratory results prior to initiating treatment.[4]

Evidence for atypical antipsychotic medication for BPSD

Atypical antipsychotic medication has the largest evidence base for efficacy in treating BPSD.[18] However, the available data are rampant with inconsistent results and are based on small RCTs with limitations, short durations (typically 12 weeks), prominent placebo response rates (30% to 40%), and highly selected patients.[14] The evidence is strongest for treatment of aggressive BPSD and weaker for nonaggressive forms.[14,19] Most studies have included only patients with Alzheimer disease and vascular dementia, making extrapolation to other forms of dementia difficult.[18] The specific behaviors of wandering, exit-seeking, and disruptive vocalizations are unlikely to respond to pharmacological treatment.[12] The number needed to treat (NNT) with atypical antipsychotic medication to improve BPSD ranges from 5 to 14.[19] There is no good evidence that atypical antipsychotic medication improves the patient's functional abilities or quality of life, or reduces caregiving time needed,[20] although improvements can be seen for some patients anecdotally.

Risks of atypical antipsychotic therapy

Risks associated with atypical antipsychotic medication are also important to consider. There has been incomplete reporting of side effects in randomized controlled trials[21] and risks after 12 weeks of use are largely unknown.[4] Adverse drug reactions include urinary tract infections (number needed to harm, NNH = 25), extrapyramidal symptoms, confusion, falls, hypotension, ECG abnormalities and peripheral edema (NNH = 20), abnormal gait (NNH = 13), and tardive dyskinesia, anticholinergic toxicity, and somnolence (NNH = 10).[19] Other adverse reactions include respiratory tract infections, hyperglycemia, weight gain, and cognitive decline.[19]

The increased risk of mortality that prompted the Health Canada June 2005 warning against the use of atypical antipsychotic medication in patients with dementia[22] is based on two meta-analyses.[23,24] The warning was unclear about whether pre-existing factors affect the risk of death, and provided insufficient information on the cause of death.[4] NNH was found to be 100 and results were pooled for risperidone, olanzapine, quetiapine, and aripiprazole.[23]

Health Canada has also warned of an increased risk of cerebrovascular events with risperidone (October 2002) and olanzapine (March 2004). These warnings were based on an independent meta-analysis that showed the NNH was 71, with a 2.2% occurrence of cerebrovascular events in the study population over a 0.8% risk in the general population.[25] Again, it is unclear if pre-existing factors affected risk.[4] Also, the overall rate of cardiovascular events did not differentiate between TIA and stroke.[4]

Despite the numerous study limitations and the known side effects of atypical antipsychotic medications, nonpharmacological interventions may not be enough to ease patient distress and caregiver burden. The VCH guideline recommends that atypical antipsychotic medications be used when

"there is a significant risk of harm to the patient or others, or when agitation or aggressive symptoms are persistent, recurrent, or severe enough to cause significant suffering and distress, or significant interference with care."[4] The NNT has been estimated from 9 to 25 when the risks of these medications are taken into account.[23] However, decisions must be made at an individual patient level and it remains difficult to predict which patients will benefit and which may be harmed.[4]

Initiating atypical antipsychotic therapy

Prior to initiating use of atypical antipsychotic medication, the prescriber should inform the family or substitute decision-maker about treatment options, risks, and benefits, obtain consent, and document the conversation.[14]

Currently, Health Canada has approved risperidone for "short-term symptomatic management of inappropriate behavior due to aggression and/or psychosis" in dementia. A Cochrane review found evidence for risperidone and olanzapine to treat aggression, and for risperidone to treat psychosis.[18] Patients with Lewy body and Parkinson disease are especially susceptible to extrapyramidal symptoms and hence quetiapine is typically recommended for these individuals.[12]

When initiating atypical antipsychotic medication, begin at a low dose (e.g., risperidone 0.25 mg per day, olanzapine 2.5 mg per day, or quetiapine 12.5 to 25 mg per day).[4] As some adverse drug reactions are dose-related (e.g., hypotension, gait disturbance, extrapyramidal side effects, somnolence, and anticholinergic side effects), "aim for the lowest effective maintenance dose."[4] Target doses have not been studied in detail,[23] but consider doses in the range of risperidone 0.5 to 1.5 mg per day, olanzapine 5 to 10 mg per day, or quetiapine 50 to 200 mg per day.[4] These medications can be given once or twice daily; any more often is probably unnecessary.[4]

As-needed dosing of atypical antipsychotic medication has not been studied in terms of efficacy or harm and has not been compared to other commonly used as-needed medication such as benzodiazepines. The VCH guideline outlines four situations for as-needed dosing of atypical antipsychotic medication: "to determine the need for a maintenance dose, during the dose titration phase in conjunction with regular dosing, in advance of unavoidable activities known to trigger significantly aggressive or agitated behavior, and for anticipated but intermittent behaviors."[4] The rationale for using single doses of atypical antipsychotic medication should be documented, as should a specific indication for use.[4] Assessment of as-needed doses should be ongoing to determine if the regular dosing should be increased.[4]

Monitoring atypical antipsychotic therapy

Monitoring has been previously described, and follow-up intervals at 1 week post initiation of treatment and 10 days after dose changes have been recommended.[26] The VCH guideline suggests that a decision regarding effectiveness should be made by 8 weeks.[4] Physical assessments should monitor for movement disorders (extrapyramidal symptoms and tardive dyskinesia).[4] Although monitoring for hyperglycemia, dyslipidemia, and weight gain has also been recommended, clinical relevance in the patient with BPSD has not been determined.[4] Atypical antipsychotic medication should be reduced or discontinued if the QTc interval becomes prolonged.[27]

Withdrawing medications

When considering the duration of atypical antipsychotic therapy in BPSD, it is important to note that most randomized controlled trials have not extended beyond 12 weeks,[28] and therefore efficacy and harm beyond this time are not well known. At least one study has shown an increase in mortality when using atypical antipsychotic medication at 3-year follow-up, but the study limitations are numerous.[28] In many patients, symptoms fluctuate as part of the disease and may attenuate as the disease progresses. For example, in patients with Alzheimer disease, hallucinations may resolve after a few months, but delusions, aggression, and agitation can persist for longer.[6,29] Given the side effects of these medications, it is reasonable to lower or discontinue their use after a period of stability. For instance, Canadian guidelines for long-term care recommend periodic attempts to taper and discontinue atypical antipsychotic medication.[12] The authors of the VCH guideline have created an algorithm with a suggested tapering schedule to begin after 3 to 6 months of behavioral stability.[4] The prescriber is advised to review a recent behavior log and if the behavior is acceptable, lower the atypical antipsychotic by the smallest dosage possible. The behavior can be revisited in 2 to 4 weeks and the dosage tapered again if the behavior remains stable. Despite these recommendations, some patients will likely need long-term therapy with atypical antipsychotic medication,[30] especially those with more severe symptoms.[27]

Pharmacological alternatives

Typical antipsychotic medications can be useful in patients who refuse oral preparations and require intramuscular injection.[31] Haloperidol and

loxapine can be used for short-term treatment, and zuclopenthixol intermediate-acting depot (Acuphase) can be used for patients with persistent and dangerous BPSD.[31]

Benzodiazepines are not typically recommended for the elderly because they increase risk of falls, fractures, and confusion.[12,32] When caring for individuals who are bed-bound and resistive to nursing procedures, fast-acting benzodiazepines such as lorazepam can aid in the completion of care without oversedating the patient.[31] Short-term use may sometimes be warranted, but long-half-life benzodiazepines such as diazepam should be avoided.[12]

Although the evidence for use of trazodone is not clear, it has been shown to be helpful in patients with agitation, anxiety, and sleep disturbance.[12] Cholinesterase inhibitors can reduce apathy, depression, and aberrant motor behavior,[17] and can be particularly useful in Lewy body disease.[12] Memantine is indicated in treatment of moderate to severe Alzheimer disease, either by itself or in conjunction with a cholinesterase inhibitor.[11,17] It has also been shown to stabilize agitation and irritability in some patients, or even prevent the emergence of BPSD,[17] but may worsen agitation in a few.

Antidepressants are another option. Symptoms can improve with SSRIs, supporting the explanation of BPSD as due in part to frontal serotonin dysfunction.[33] Citalopram and sertraline have the best evidence for use in patients with dementia.[12,17,34] The patient should be monitored for syndrome of inappropriate antidiuretic hormone secretion after SSRI therapy begins, and a baseline sodium excretion value should be obtained.

There is also evidence for using anticonvulsants in BPSD. However, studies of valproic acid, carbamazepine, oxcarbazpine, and gabapentin have shown conflicting results.[11] Gabapentin dosing must be reduced in those with renal impairment.

Medications used for BPSD that have a poor evidence base include analgesics (unless there is a clear pain syndrome, or incident pain during personal care),[35] cannabinoid receptor agonists (nabilone and dronabinol), and hormonal treatments (antiandrogen agents, melatonin, and ginkgo biloba extract).[31]

Clinicians should be aware that aggressive forms of BPSD are more responsive to atypical antipsychotic medication than are nonaggressive forms, and that other forms of pharmacotherapy can also be useful.

Conclusions

Behavioral and psychological symptoms of dementia eventually occur in more than 90% of patients with dementia and can severely affect the patient's quality of life and increase caregiver stress. The Vancouver Coastal Health Authority has recently produced a guideline that addresses the assessment and management of BPSD with atypical antipsychotic medication. The guideline recommends evaluating patient's symptoms within a biopsychosocial model and treating all reversible causes of BPSD prior to initiating pharmacological therapy. Clinicians should be aware that aggressive forms of BPSD are more responsive to atypical antipsychotic medication than are nonaggressive forms, and that other forms of pharmacotherapy can also be useful.

Competing interests

None declared.

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