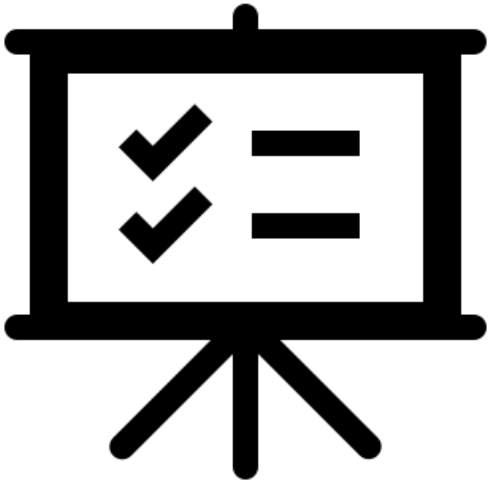
Pharmacological management of behavioral & psychological symptoms of dementia, part 2

this content is up-to-date as of

May 3, 2021

Wisconsin Alzheimer's Institute
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Learning objectives



- Develop an algorithm for managing BPSD
- List the risks and benefits of using the following medications/classes for BPSD: antidepressants, anticonvulsants, benzodiazepines, stimulants & others

Overview of management

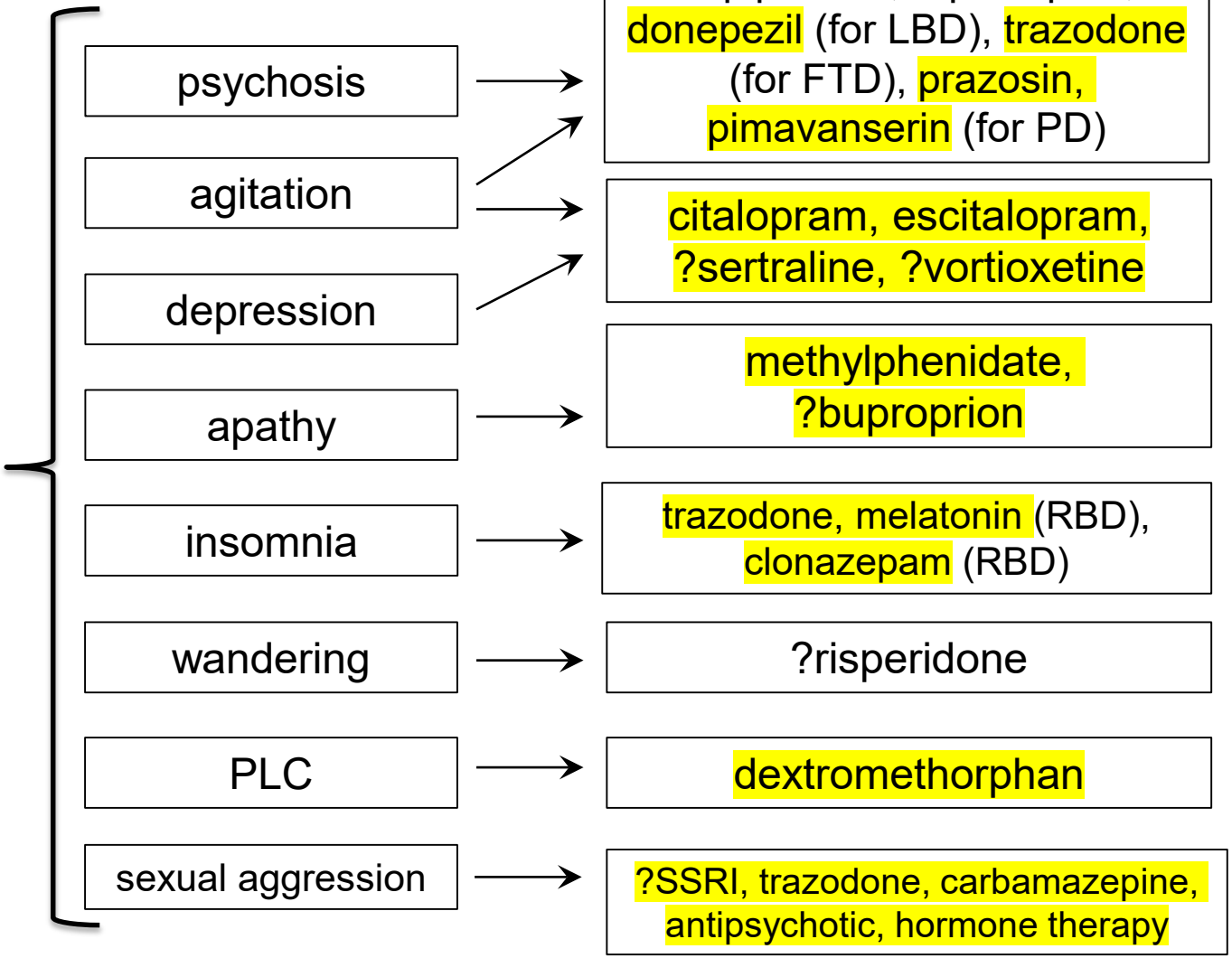
- treat underlying medical causes
- discontinue offending medications & substances
- support & educate caregivers & other family members
- develop a psychological, behavioral & environmental management plan
- avoid adding new medications, unless there is risk of harm to patient or others
- if a medication is added, regularly monitor outcomes & attempt discontinuation
- ensure that patients & caregivers are in a safe environment

Walaszek *Behavioral & Psychological Symptoms of Dementia* 2019.

Start low, go slow

Specific BPSD

Implement caregiver, behavioral & environmental interventions first; if ineffective and BPSD dangerous or distressing…



Walaszek *Behavioral & Psychological Symptoms of Dementia* 2019. FTD = frontotemporal dementia, LBD = Lewy body disease, PD = Parkinson disease, PLC = pathological laughing & crying, RBD = REM sleep behavior disorder.

Antidepressants (1)

- best risk-benefit profile of any drug class for pharmacological treatment of BPSD, specifically of agitation and depression
- **citalopram** 30 mg/d has the strongest evidence for efficacy for agitation, but it is associated with QT prolongation
- **escitalopram** may be effective, without QT prolongation as a side effect and with good cardiac safety
- **sertraline:** after initial (50-150 mg/d) for treating depression, more recent trials have not demonstrated efficacy (but well tolerated)

Farina et al., *Int J Geriatr Psychiatry* 2017; 32:32–49.

Antidepressants (2)

- **trazodone:** fairly strong evidence base for agitation in frontotemporal dementia; start 25-50 mg/d, titrate up to 250 mg/d as tolerated
- **bupropion:** very little evidence, but could be considered for apathy (though most recent study was negative); antidepressant least likely to cause hyponatremia
- **mirtazapine:** negative trials, but could be considered for insomnia or anorexia
- **duloxetine, fluoxetine, venlafaxine:** negative trials or very little evidence of efficacy
- **paroxetine, tricyclic antidepressants:** avoid, due to anticholinergic side effects
- **vortioxetine**: maybe beneficial for cognition as well as mood

Farina et al., *Int J Geriatr Psychiatry* 2017; 32:32–49; Maier et al., *JAMA Netw Open* 2020; 3(5):e206027; Cumbo et al., *J Prev Alzheimers Dis* 2019; 6(3):192-197..

Antidepressants (3)

- safety concerns
  - hyponatremia
    - risk factors include: female gender, age > 65, use of diuretics
    - possible with any antidepressant, but least likely with bupropion (and perhaps mirtazapine)
    - check baseline sodium, then 2-3 weeks after starting and after each dose increase
  - QT prolongation: citalopram
  - falls
  - GI side effects, weight loss

Other pharmacological options (1)

Medication	Comments
acetaminophen	consider for all patients with BPSD, 1000 mg twice or three times daily
carbamazepine	risks include drug-drug interactions, hyponatremia, neutropenia/agranulocytosis
clonazepam	avoid, except in REM sleep behavior disorder
dextromethorphan	best evidence for pathological laughing & crying, combined with quinidine to increase half-life
donepezil	first choice for Lewy body disease, otherwise likely not effective for BPSD
gabapentin	very little evidence to support use
lorazepam	avoid, except in emergency situations

Walaszek *Behavioral & Psychological Symptoms of Dementia* 2019.

Other pharmacological options (2)

Medication	Comments
melatonin	1-3 mg 2-3 hours before bedtime, not likely to be effective except perhaps for REM sleep behavior disorder
memantine	not likely to be effective for BPSD
methylphenidate	for apathy, start at 5 mg morning & noon, titrate to 10 mg morning & noon, monitor blood pressure
pimavanserin	only for psychosis associated with Parkinson disease, may increase mortality
prazosin	one small study indicated efficacy, start 1 mg qhs, may increase to 2 mg qam and 4 mg qhs
valproate	do not use

Walaszek *Behavioral & Psychological Symptoms of Dementia* 2019.

Summary: managing BPSD (1)

1. Is there imminent risk of harm to the patient or others?
   - yes: activate emergency medical system
   - no: proceed with next step
2. Treat underlying medical causes, including pain
3. Discontinue offending medications or substances
4. Are BPSD severely distressing to patient or potentially dangerous to patients or others?
   - no: implement caregiver, behavioral and environmental interventions
   - yes: proceed with next step on next slide

Summary: managing BPSD (2)

5. Is patient taking psychotropic medication for BPSD?
   - yes: maximize current medication; if already at recommended dose, switch to another medication
   - no:
     - agitation: SSRI, trazodone, atypical antipsychotic, prazosin
     - psychosis: antipsychotic
     - Lewy body disease: donepezil, clozapine, pimavanserin
     - depression/anxiety: SSRI, ?vortioxetine
     - apathy: methylphenidate
     - pathological laughing/crying: dextromethorphan
     - any: acetaminophen

Summary: managing BPSD (3)

6. For all medication recommendations:
   - obtain informed consent (usually from proxy decision maker)
   - titrate at appropriate pace to appropriate dose
   - monitor outcome
   - continue non-pharmacological interventions
   - consider eventually discontinuing, especially antipsychotics (see *Deprescribing* slide set)