Evidence Based Algorithmic Psychopharmacological Approach to Behavioral and Psychological Symptoms of Dementia (BPSD)

**BACKGROUND:**
- Dementia affects 5 million adults over 65yr, projected to affect 3.3% of population by 2060 [1].
- BPSD include screaming, calling out, verbal and physical aggression, agitation, apathy, sexual disinhibition, defecation, wandering, hostility, and paranoid behaviors, psychosis, and mood disorders- bolded are most seen clinically [2-6].
- BPSD associated with poor prognosis, accelerated decline in cognition and quality of life [6]
- 80% of those with dementia will experience BPSD [7].
- BPSD lead to caregiver burden, and frequently becomes the reason patients are admitted to nursing homes [4-6]

**METHODS:**
- BPSD and Nonemergent Management [2018: 12 articles reviewed]
- BPSD and Antipsychotics since 2018: 11 articles reviewed
- BPSD and Psychopharmacology since 2018: 11 articles reviewed
- BPSD and Parkinson's Disease: 2 studies in 2012
- Prazosin: 2013: 4 articles reviewed
- BPSD and Antidepressants
- Prazosin and Alzheimer's Disease: 2 studies in 2012
- BPSD and Anticholinergics
- Second Generation Antipsychotics
- BPSD and Atypical Antipsychotics
- Second Generation Antipsychotics
- Trazodone
- Escitalopram
- Donepezil
- Olanzapine
- Quetiapine
- Clozapine
- Aripiprazole
- Lithium
- Risperidone
- Rasagiline
- Benznidazepine
- Prasradal
- ECT

**Key Points:**
- Manage BPSD early. We hope that our non-emergent psychopharmacological management will keep patients from entering the emergent pathway.
- Pharmacological management can be necessary and helpful
- In a non-emergent setting, fast and positive response to agitation and paranoia suggests favorable response to antipsychotic use in the future [18].

**Why this matters:**
- Correct decision on pharmacological approach can potentially shorten duration of BPSD, enhancing quality of life for both patient and caregiver.
- Our patient population is aging and BPSD management likely will become more common in clinical practice.

**Take Away**
- Aripiprazole is the most evidenced based pharmacological management option for emergent BPSD
- When deciding management strategy it is important to consider if this is emergent or not, and remember to take into account of patient history to help in clinical decision making process.
- Valproic acid, benzodiazepines, and olanzapine should be avoided in BPSD management, especially non-emergent situations.

**Algorithm**

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<tbody>
<tr>
<td>Emergent</td>
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<tr>
<td>Non Emergent</td>
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<tr>
<td>M/O Antidepressant</td>
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<tr>
<td>Antipsychotic</td>
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<td>Risperidone</td>
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**References:**

**Rationale**

**Emergent**

1. **Antipsychotic**
   - Only realistic intranasal injection on market
   - Supported by 1 meta analysis of 17 studies, concluding Aripiprazole to be most efficacious and safe [11]
   - Dosing: Initiate at 1mg/d, titrate to maximum of 20mg/d [6]

2. **Support with Anticholinergic**
   - Approved BPSD in Australia & UK, also approved for aggression and psychosis symptoms for Alzheimer’s in Canada [10]
   - Supported by 5 large randomized control trials [10] and 1 systematic review [10]
   - tetrahydrobiphenyl side effect profile
   - Avoid in Parkinson’s and Lew Body Dementia [11], watch out for cardiovascular disease [10]

3. **Quetiapine**
   - Supported by 1 meta analysis of 5 randomized trial [8]
   - Efficacious for agitation [8]
   - Quetiapine is ranked lower than aripiprazole due to its high anticholinergic properties
   - Recommended starting at 12.5mg at night, with slow titration to 30mg maximum daily [6]

**Non-Emergent**

1. **Antidepressant**
   - General should be avoided due to association with poor outcomes with falls, cognitively, and BPSD exacerbation [2,25]
   - Many have agreed that it can be used for extreme BPSD presentations (8,15) and special circumstances like medical procedures (8)

2. **Prazosin**
   - Supported by 1 randomized control trial [12], 2 clinical trials with favorable results.
   - Dose range: 1-5mg/day
   - Recommended using at 1-2mg/day with possible sympathomimetic benefit

3. **Escitalopram**
   - Ranked above clozaprida due to more favorable cardiac profile
   - Recommended starting at 10mg daily [13]
   - Clozapine
   - Supported by 4 randomized control trials [8]
   - Slow to see effect, around 5 weeks [8]
   - Helpful in context of depression [12]
   - Need to monitor (UGL)

4. **Sertraline**
   - Show to be efficacious from 50-200mg [12]
   - Trandolapril
   - Does off labeled use for BPSD over 20mg, minimal anticholinergic properties, mostly histamineergic [8]
   - Recommended to use at 12.5mg-25mg [13]
   - Supported by 2 CMAX trials, not inferior to haloperidol for agitation treatment, and less side effects [9]

5. **Carbamazepine**
   - Supported by 2 small studies with positive results [11]
   - Use with caution, requires frequent hepatic enzyme monitoring, frequent complete blood count monitoring [10]
   - For this reason it is recommended only after galperpine.

6. **Cannabidiol**
   - Evidence seems mixed right now for therapeutic benefit [8]
   - Many small studies showing positive results
   - Valproic Acid
   - In a 24 month multi site RCT, shown to be ineffective, with multiple side effects [14]
   - Studies overall do not support use of valproic acid in this population [15]

7. **Clonazepam**
   - Avoid in BPSD due to metabolic and anticholinergic properties; in addition anti-agitation effects not shown in placebo controlled trial [8]
   - Increased risk of cardiovascular disease [10]
   - Network meta analysis showed olanzapine had least BPSD benefit of all atypical antipsychotics and increased cardiovascualr adverse events [11]

8. **Subanephrin**
   - Helpful in context of neuropathic pain
   - Supported by 14 case reports showing positive effects [14]
   - On average, needs 2 weeks to see full effect [8]
   - Works poorly in Lew Body Dementia and wide range of efficacious dose (200mg-3000mg) [14]
   - May add to clonazepam because it can be beneficial from further studies.

**Conclusion:**
To our knowledge, this algorithm provides the most up to date and evidenced based approach to help with BPSD management.
- Current literature on BPSD is largely focused on Alzheimer’s and vascular dementia.
- If algorithm is proving to be unhelpful, amongst other things, prudent to re-examine diagnosis.
- This field will benefit from whether BPSD treatment response will be different amongst dementia types.

**AUTHORS:**
- Anderson Chen M.D.1,2, Frank Capelli M.D.1,2, Alexis A. Cloutier D.O.1,2, David OssenM.D.1,2
- 1=Harvard Medical School
2= VA Boston Healthcare System