Management of Behavioral Disturbance in Dementia: Complexities in Antipsychotic Use

The Quality Equation
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Behavioral Effects and Medication in the Elderly

Science of placebo effect
- Elderly samples have profound placebo effects
- Activation of serotonergic pathways has been observed in an antidepressant study using placebo
- Dopamine release occurs in anticipation of reward
- Depends on conditioning, expectations, meaning and context of the treatment, patient-provider interactions

Cherniack EP. Would the elderly be better off if they were given more placebos? Geriatr Gerontol Int. 2010 Apr;10(2):131-7.

Outcome Measures

- Placebo Effects
- Geriatric psychiatry = Off label prescribing
- How do we identify and measure the most appropriate outcomes?
- How can mental health providers document progress in achieving optimal care outcomes?
  - Understanding not just drug trials, but the context of care, patient-provider, patient-centered goals

Normal Older Adults: 4 Groups

<table>
<thead>
<tr>
<th>APOE e4+</th>
<th>APOE e4-</th>
</tr>
</thead>
<tbody>
<tr>
<td>e4+ genotype disclosed</td>
<td>e4- genotype disclosed</td>
</tr>
<tr>
<td>e4+ genotype not disclosed</td>
<td>e4- genotype not disclosed</td>
</tr>
</tbody>
</table>

- APOE E4+ and E4- groups did not differ cognitively
- E4+ disclosed scored ↓ than E4+ not disclosed
  - logical memory immediate and delayed recall
- E4+ not disclosed did not differ from the two E4- groups.

Perception and Environment

- Cognitive testing and expectations of outcome in older adults
  - Cognitively NORMAL older adults who are APOE e4 positive
    - And are told they are positive
  - Perform WORSE on both subjective and objective cognitive testing
  - Compared to other people who are also APOEe4 positive but are NOT told

Expectations and Hope

• Phase I outcomes from the CATIE-AD effectiveness trial:
  – Clinicians tended to switch to another study drug (i.e.,
    advance participant to Phase II) even when there were
    slight improvements
  
• Relapse risk after discontinuation of risperidone in Alzheimer’s disease
  
• Evidence for worsening with discontinuation
  • Pan et al., Dement Geriatr Cogn Disord 2014

Importance of Target Symptom Approach

• Investigated weekly changes within Phase I
  – Olanzapine and risperidone patients (compared to placebo) more improvement in NPI total score
  – Risperidone = improvement on the CGIC
  – Olanzapine and risperidone = improvement on the BPRS hostility suspiciousness factors
  – Risperidone = improvement on BPRS psychosis factor
  – Worsening with olanzapine on BPRS withdrawn depression factor

Cochrane Review Summary

• Atypical Antipsychotics for Aggression and Psychosis in Alzheimer’s disease
  – Ballard C, Waite J, Birks
  • Cochrane Database of Systematic Reviews (2006) Issue 1
  • 16 studies through 2004, all placebo controlled
  • Main Results
    – Improvement in aggression with risperidone and olanzapine compared to placebo
    – Improvement in psychosis with risperidone compared to placebo

Signals of Medication Effects

• The significant findings in the updated review include small but statistically significant benefits for olanzapine,
  aripiprazole, and risperidone for elderly patients with dementia
  – “Conclusions could not be drawn by the reviewers as to the minimum dose needed to achieve efficacy”
    Maher AR et al., J. Manag Care Pharm 2012 (5) Suppl B: S1-20

  • CATIE AD: Mean doses reached in Phase I
    • Olanzapine 5.5 mg/day
    • Quetiapine 56.5 mg/day
    • Risperidone 1.0 mg/day

Antipsychotic Selection and Monitoring for Behavioral Disturbances in Dementia

1. Rule out medical source/delirium, use non-drug options first.
2. Avoid using antipsychotics for inappropriate treatment targets, as per CMS regulations.
3. Target symptom(s) must present a danger to the resident or others, or
   be significant enough that the resident is experiencing one or more of
   the following: inconsolable or persistent distress, a significant decline
   in function, substantial difficulty receiving needed care.

Potentially appropriate treatment targets:
- Aggressive behavior (especially physical)
- Hallucinations
- Delusions (note: memory problems are often mistaken for delusions, e.g. if the person is usually very quiet and talkative, assume delusional behavior)
- Other acute distress that meets the criteria in #1 in general guidelines

Inappropriate treatment targets:
- Wandering
- Uncooperativeness
- Place self-care
- Restlessness
- Impaired memory
- Sleep disturbance or intolerance to surroundings
- Verbal expressions or behaviors that do not represent a danger to the resident or others

The long-term effects of conventional and atypical antipsychotics in patients with probable AD

1. Lopez OL, et al.
   “The use of antipsychotic medications, both conventional and atypical, was not associated with either time to nursing home admission or time to death after adjustment for relevant covariates. Rather, it was the presence of psychiatric symptoms, including psychosis and agitation, that was linked to increased risk of institutionalization and death after adjustment for exposure to antipsychotics.”
    » Am J Psychiatry. 2013 Sep;170(9):1051-8
Draft Recommendations

• Behavioral approaches have positive effects, are not presently adequately utilized in practice.
  – Barriers related to workforce and training need to be assertively addressed through both policy changes and research to address the lack of systematic use.
• Evidence shows that antipsychotics may have modest effects particularly for psychosis in dementia.
• A target symptom approach with close involvement with an interprofessional team and family is suggested.
  – Lowest effective dose, frequent monitoring and tapering as appropriate are suggested. Attention to costs is needed.

The Quality Equation

• Balancing quality of life
• Expectations, needs, goals of care
  – Care that matches patient’s values, life story
  – Communication with family about risks, benefits, harm in context of individual morbidity and safety
  – Interprofessional engagement, patient and family engagement = beneficence in care

QUESTIONS?