
Background:

- Agitation or psychosis is common in AD
- These sx are associated with distress, caregiver burden, risk of institutionalization, cost
- Non pharmacologic strategies recommended; little evidence to evaluate effectiveness
- Among psychotropic medications, only anti-psychotics have shown benefit over placebo for psychosis and agitation/aggression
  - Risks of sedation, PD, metabolic syndrome, afib
  - Mortality as high as 1.6 times placebo
- Some studies have found low rates of relapse following discontinuation
  - Ultra long term use (yrs) with poorly documenting initiating complaint
  - Initial response to drug rarely documented
  - Multiple drugs discontinued together
- At least one study of haloperidol responders found a high rate of relapse after discontinuation

Hypothesis:

The relapse rate will be lower in patients who continue risperidone than in patients who switch to placebo

Methods:

See Fig 1. Highlights:

- Initial 16 week response rate to risperidone 112/180 =62%
  - 0.25mg to 3mg dose allowed during phase A
- Participants - Table 1
  - Memory clinics, Geripsych clinics, VA clinics, physician referral
  - Dementia by DSM-IV, AD by NINCD/Alzheimer’s Assn criteria, psychosis/agitation by NPI
- Outcomes
  - NPI score reduced by >30%, CGI-C scores
  - Extrapyramidal sx scores, PSMS functional score, MSSE cognitive
  - Patients who died were considered to have relapse
Results:

Relapse rates: Fig 2  Highlights

In Phase B 1-16  24/40 patients in group 3 relapsed (60%), as opposed to 23/70 in groups 1-2 (33%)
   Hazard ratio 1.94 (1.09-3.45, p=0.02)

In phase B 17-32  13/27 in group 2 relapsed (48%), versus 2/13 in group 1 (15%).
   Hazard ratio 4.88 (1.08-21.98)

Side effects (Table 3) No differences

Discussion/Conclusions:

In patients who initially responded to risperidone, discontinuation was associated with an increased risk of relapse for at least 4 months.

Risperidone is not highly effecting in achieving or sustaining a reduction in psychosis or agitation in AD

- Rates of discontinuation for any reason:
  - 38% in Phase A
  - 68% in Group 1 during 32 weeks, 29% in Group 2 during first 16 weeks

Little harms of treatment in this population over 48 weeks.

Little evidentiary support for CMS mandate in NH of discontinuation of antipsychotics after 3-6 months of treatment

Practice Implications (MAF opinion)

Documentation is critical to performance evaluation

- Presenting symptoms
  - “Clinical Trial” of high risk medication – specify duration, try to quantitate outcomes
  - Re-document at intervals
  - Efficacy/effectiveness reality checks. Will continue to need a multifactorial approach to management of these challenging patients.