Haloperidol and agitation in Alzheimer’s Disease

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Psychotic symptoms (e.g. hallucinations and delusions), agitation and aggressive behavior are common in patients with Alzheimer’s Disease.  Delusions and hallucinations in Alzheimer’s Disease are typically simple and isolated, in contrast to the complex elaborated psychotic symptoms seen in schizophrenia.  Psychosis and disruptive behavior become more frequent as dementia progresses and may herald a more rapid downhill course.  Agitation, aggression, and psychosis cause physical injury as well as psychological morbidity, are upsetting to patients, and highly stressful for their caregivers.  Unmanaged, such behaviors result in nursing home placement and hospitalization, and sometimes chronic institutionalization.  Antipsychotic drugs have been widely prescribed for demented patients for many years.  Concerns have been raised regarding overuse of antipsychotics, particularly in nursing homes, and because of the risk of movement disorders, particularly tardive dyskinesia.  Demented patients appear more sensitive to extrapyramidal side effects.  Previous controlled trials have shown some benefits of antipsychotic medication for treatment of psychosis and disruptive behavior in dementia, but have a number of methodological flaws.

Devanand and colleagues conducted a six week randomized placebo-controlled trial of haloperidol in 71 outpatients with Alzheimer’s disease at two dose levels, 2-3 mgs/day (“standard dose”) and 0.50-0.75 mgs/day (“low dose”).  In a second crossover phase of six weeks, patients receiving placebo were switched to
haloperidol at one of the two doses, and patients receiving haloperidol were switched to placebo. Standard dose haloperidol was more effective in reducing psychosis and disruptive behavior, with a response rate of 55-60% compared to low dose haloperidol (25-35%) and placebo (25-30%). The superiority of the standard dose was replicated in the crossover phase. About 20% of the patients receiving the standard dose developed moderate to severe extrapyramidal signs.

This study suggests that haloperidol at a dose of 2-3 mgs/day is effective and well tolerated by most patients, and that doses below 1 mg/day are ineffective. While there are newer “atypical” neuroleptics that are less likely to cause extrapyramidal side effects, they are significantly more expensive, not yet available for parenteral administration, and they have other side effects that may be problematic in elderly demented patients (e.g. orthostatic hypotension). However, the next paper highlights a serious drawback to chronic administration of haloperidol and other conventional antipsychotics.