Pharmacological Management of Agitated Behaviors in Cognitively Impaired Older Persons

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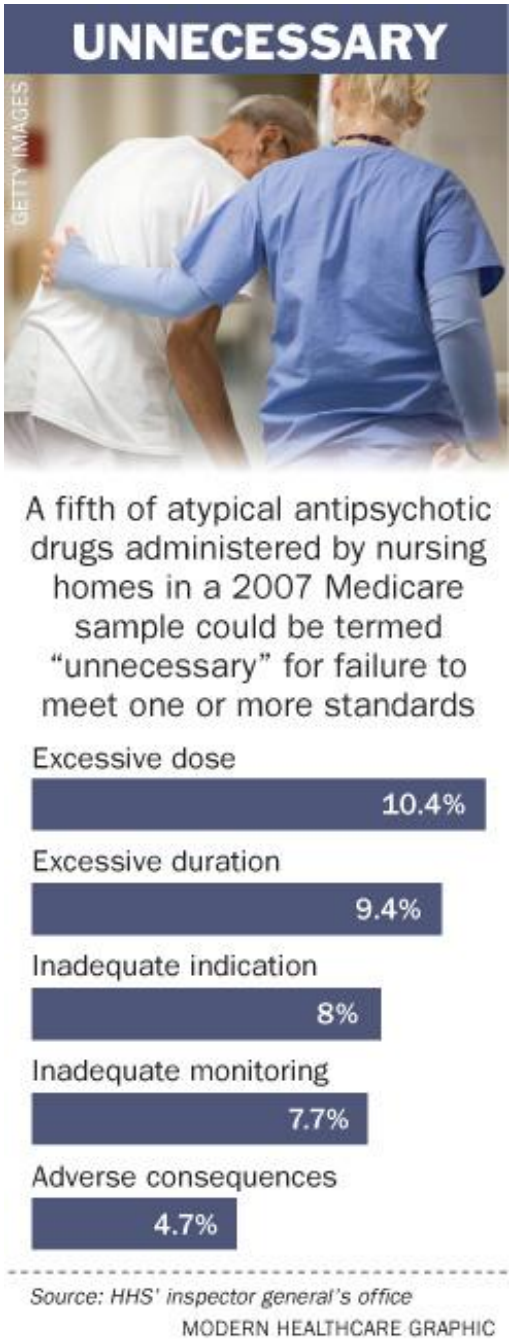
HHS IG's Report May 9, 2011

- ½ antipsychotics with no medical indication
- 14% SNF residents > age 65 on antipsychotics in 2007
- 83% were for off-label uses, or for conditions other than schizophrenia or bipolar disorder
- 22% of the atypical antipsychotic drugs administered, amounting to $63 million, were deemed unnecessary by CMS standards

http://oig.hhs.gov/oei/reports/oei-07-08-00150.pdf



HHS IG's Report May 9, 2011: "We Recommend That CMS…."

- Facilitate access to information necessary to ensure accurate coverage and reimbursement determinations.
- Assess whether survey and certification processes offer adequate safeguards against unnecessary antipsychotic drug use in nursing homes.
- Explore alternative methods beyond survey and certification processes to promote compliance with Federal standards regarding unnecessary drug use in nursing homes.
- Take appropriate action regarding the claims associated with erroneous payments identified in our sample.

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The "Compendia"

- For drugs to qualify for Medicare Part D reimbursement, the Medicare Benefit Policy Manual and the Prescription Drug Benefit Manual require that drugs be used for medically accepted indications.
- These indications include both the uses approved by FDA and those uses, including off-label, supported by one or more of three compendia:
  - the American Society of Health System Pharmacists, Inc.'s, American Hospital Formulary Service Drug Information
  - the United States Pharmacopeia-Drug Information
  - Thomson Reuters' DrugDEX Information System

CMS defines unnecessary drugs as those that are used:

- in excessive dose
- for excessive duration
- without adequate monitoring
- without adequate indications for use, and/or
- in the presence of adverse consequences that indicate that the dosage should be reduced or discontinued

State Operations Manual Pub. 100-07, Appendix PP: Guidance to Surveyors for Long Term Care Facilities, F329, § 483.25(l), Unnecessary Drugs.

- However, Medicare drug reimbursement policy does not consider payments erroneous for "unnecessary drug regimens", because drug claims are paid by or on behalf of individual residents, not nursing homes.

HHS IG's Report
May 9, 2011

- **51% of Medicare atypical antipsychotic drug claims for elderly nursing home residents were erroneous, amounting to $116 million.**
- For the period of January 1 through June 30, 2007, they determined from medical record review that over 726,000 of the 1.4 million atypical antipsychotic drug claims for elderly nursing home residents did not comply with Medicare reimbursement criteria. The claimed drugs were either not used for medically accepted indications as supported by the compendia (50.2%) or not documented as having been administered (0.3%) to the elderly nursing home residents.

Where are we?

- Many families of medications have been proposed for managing agitated behaviors in dementia
- Most that have been studied adequately fail to differentiate from placebo
- The best data for efficacy remains that reported for the antipsychotics – NNT≈7
- Unfortunately, the side effects of these medications include death and cognitive impairment
- The data supporting other medications – antidepressants, cholinesterase inhibitors, valproate, etc. is much weaker or non-existent

Cognitive effects of Atypical Antipsychotics

- In CATIE-AD, atypical antipsychotics were associated with worsening cognitive function at a magnitude consistent with 1 year's deterioration compared with placebo.
- For comparison, RCT data show only a 3-6 month's worth cognitive function improvement with cholinesterase inhibitors
- Drugs in CATIE-AD were olanzapine, quetiapine, and risperidone

Vigen CLP et al. Cognitive Effects of Atypical Antipsychotic Medications in Patients With Alzheimer's Disease: Outcomes From CATIE-AD. Am J Psychiatry. 2011 May 15;

Excess Mortality with Atypical Antipsychotics

- Odds ration of death in randomized, placebo-controlled trials (≈ 3300 patients) was 1.54
- Number-needed-to-harm = 100 (95% CI 53-1000)
- NNT ranged from 4-12 – therefore for every 9-25 people helped there was one excess death

Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. JAMA. 2005 Oct. 19;294(15):1934-1943.

- If anything, risk with typical antipsychotics is worse

Musicco M, Palmer K, Russo A, Caltagirone C, Adorni F, Pettenati C, et al. Association between Prescription of Conventional or Atypical Antipsychotic Drugs and Mortality in Older Persons with Alzheimer's Disease. Dement Geriatr Cogn Disord. 2011;31(3):218-224.

Antipsychotics

- Best up-to-date review:
  - Ballard C, Creese B, Corbett A, Aarsland D. Atypical antipsychotics for the treatment of behavioral and psychological symptoms in dementia, with a particular focus on longer term outcomes and mortality. Expert Opin Drug Saf. 2011 Jan. 1;10(1):35-43.
- Need to balance modest efficacy versus 1.5-1.8x mortality rate in 12 week studies – longer term excess mortality less well defined but likely present
- In general, best practices would be to use antipsychotics much less often than in past

CA Regulations Re Antipsychotics

- Health and Safety Code (HSC) Section 1418.9(a) states:
  - "If the attending physician and surgeon of a resident in a skilled nursing facility prescribes, orders, or increases an order for an antipsychotic medication for the resident, the physician and surgeon shall do both of the following:
  - (1) Obtain the informed consent of the resident for purposes of prescribing, ordering, or increasing an order for the medication. (2) Seek the consent of the resident to notify the resident's interested family member, as designated in the medical record. If the resident consents to the notice, the physician and surgeon shall make reasonable attempts, either personally or through a designee, to notify the interested family member, as designated in the medical record, within 48 hours of the prescription, order, or increase of an order."

CA Regulations Re Antipsychotics

- CCR Title 22 Section 72528(e): "There shall be no violation for initiating treatment without informed consent if there is documentation within the patient's health record that an emergency exists where there is an unanticipated condition in which immediate action is necessary for preservation of life or the prevention of serious bodily harm to the patient or others or to alleviate severe physical pain, and it is impracticable to obtain the required consent, and provided that the action taken is within the customary practice of licensed healthcare practitioners of good standing acting within the scope of their professional licensure in similar circumstances.

Antipsychotics and NPs or Pas in SNFs

- HSC Section 1418.9(a), stipulates that a physician or a surgeon shall obtain the informed consent of a resident
- This is a statute; it overrides regulations… so in a SNF a Licensed Practitioner other than a physician can not order antipsychotic medications and you would need a physician or surgeon to obtain the informed consent.
- HSC Section 1418.9(b)(4) “Increase of an order" means an increase of the dosage of the medication above the dosage range stated in a prior consent from the resident.”

What Next?

- Remember that the placebo effect in clinical trials is very high – very few active treatments have been shown to exceed it.
- Consider lowest toxicity treatment if treatment is indicated but not urgent:
  - Aromatherapy?
  - Buspirone?
- Cholinesterase inhibitors and memantine have not been shown to have anti-agitation efficacy in clinical trials of agitated patients, but may be worth considering if otherwise indicated

Antidepressants for Agitation in AD

- Relatively small number of studies evaluating the effects of antidepressants on symptoms of agitation and psychosis in dementia with only nine studies meeting inclusion criteria.
- Two studies of found some benefit of citalopram and sertraline for treating NPS of dementia when compared to placebo.
- Several other studies found no difference of efficacy compared to antipsychotics

Seitz DP, Adunuri N, Gill SS, Gruneir A, Herrmann N, Rochon P. Antidepressants for agitation and psychosis in dementia. Cochrane Database Syst Rev. 2011;2:CD008191.

Valproate

- No evidence of efficacy
- Black box warnings for fatal hepatotoxicity, pancreatitis and teratogenicity

Lonergan E, Luxenberg J. Valproate preparations for agitation in dementia. Cochrane Database Syst Rev. 2009;(3):CD003945.

Benzodiazepines

- No evidence of efficacy
- Fall risk
- Worsening of cognitive impairment
- Withdrawal phenomenon
- Should be used rarely if at all

- "Benzodiazepines are good for delirium" ☺

Short-acting Benzodiazepines versus other Strategies for the Management of Agitation in Older Patients: Clinical Effectiveness and Guidelines. Source: **Canadian Agency for Drugs and Technologies in Health (CADTH)** Health Technology Assessment published 6/28/2010

Final Thoughts

- Step back and analyze where "push" for pharmacotherapy is coming from – is it because of resistance to care, for vocalizations distressing to others or physical aggression that is dangerous to others, or is there strong evidence that the resident themself is experiencing distress.
- Redouble efforts to manage environment and interactions with resident to handle behaviors without medications if possible
- If ever documentation of your thought process was important, the use of medications for behavioral management in dementia is it.

Final Thoughts

- If antipsychotics are considered, ask yourself and then the responsible party – "Is a 1 out of 7 chance that I will improve these symptoms (compared to placebo use) worth a 1/100 chance I will cause a death over the next 12 weeks?"
- If the answer is "yes", document this discussion. I suggest documenting a dose range that is not associated with excess morbidity e.g no more than 2 mg risperidone. That way if higher dose is needed, you will be forced to document discussion of the higher risks of sedation and other side-effects.