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How should dementia with psychosis be treated?

Many—if not most—psychiatrists treating dementia-related psychosis in geriatric patients use second-generation antipsychotics (SGAs), a practice not approved by the FDA. Consider the following 2 emergency consultation cases:

- Mrs. A, age 76, has exhibited serious memory difficulties for >1 year. She can no longer find her way home or take care of personal needs. This morning her husband brings her to the ER after she struck him on the head with a frying pan and threatened to kill a 72-year-old widowed neighbor with whom she accused him of having an affair.
- Mr. J, age 82, was diagnosed with Alzheimer's disease 3 years ago and resides in a nursing home. You receive a call from staff that Mr. J has become very agitated, accused his roommate of stealing his belongings, and screamed at the roommate and staff to give him his "stuff" back.

These 2 vignettes describe classic cases of psychotic symptoms occurring in the context of dementia. Both patients clearly need an antipsychotic to control their delusions and prevent them from endangering themselves and others.

The mortality risk of SGAs vs FGAs is what really matters to clinicians who prefer SGAs but are intimidated by the black-box warning

SGAs vs FGAs vs placebo. Late-life dementia is associated with a 50% incidence of psychosis. These patients are extremely susceptible to neurologic movement disorders (acute parkinsonism and subsequent tardive dyskinesia [TD]) when given first-generation antipsychotics (FGAs) and far less so with SGAs. After 9 months' exposure, geriatric patients with psychotic symptoms have been shown to be 10 times more likely to develop TD with FGAs (28%) than with SGAs (2.5%).[1]

Even so, in 2005 the FDA imposed a "black-box" warning on the use of SGAs for psychosis related to dementia because the mortality rate in 17 pooled placebo-controlled dementia studies was approximately 1.7 times higher with SGAs (4.5%) compared with placebo (2.5%).[2] Causes of death were mostly heart-related or pneumonia.

When treating psychosis in the elderly, however, we don't choose between an SGA and placebo but between SGAs and FGAs. Thus, the

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relative mortality risk of these 2 drug classes is what really matters to clinicians who prefer to use SGAs but feel inhibited by the black-box warning.

New evidence. Many practitioners might not be aware that 4 studies published since 2004 of elderly patients receiving antipsychotics have addressed the relative risk of mortality with SGAs vs FGAs. In patients age ≥65 with dementia, these studies found:

- In a 2-year U.S. retrospective review, the mortality rate was 21% among those receiving haloperidol vs approximately 5% among those receiving risperidone or olanzapine.[3]
- In a retrospective U.S. study of 2,890 patients who started FGAs or SGAs between 1994 and 2003, FGAs were at least as likely as SGAs to increase the risk of death. The greatest increases in risk were seen soon after patients started antipsychotic therapy and with higher dosages of FGAs.[4]
- In a 2-year prospective study of 254 very frail patients (mean age 86) in Finnish hospitals or nursing homes, neither the use of FGAs nor SGAs increased the risk of death or hospital admission. The use of restraints, however, doubled the risk of death.[5]
- In a population-based, retrospective Canadian study of 27,259 matched pairs, a statistically significant increase in mortality was seen with SGAs compared with no antipsychotic use, whether patients lived at home or in longterm-care facilities. This difference was seen 30 days after treatment started and seemed to persist to 180 days. By comparison, the mortality risk appeared to be higher with FGAs than with SGAs at all measured time points.[6]

The black-box warning on SGAs does not guide clinicians in the use of antipsychotics; it simply compares a class of drugs with placebo, and sugar pills are not an option for managing psychosis. The 4 published studies represent a more useful guide about the relative mortality risk of FGAs and SGAs. They also provide evidence that supports clinical practice in managing patients with psychosis in late-life dementia.

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