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Editor-in-Chief

Older patients with delirium routinely are treated with antipsychotics, but those with dementia are not

The delirium/dementia treatment paradox

Delirium is the most common psychiatric disorder on medical/surgical units of general hospitals and is a major cause of consultations for consultation-liaison (C-L) psychiatrists in medical centers.

It primarily afflicts older patients and is characterized by a rapid onset of confusion with hallucinations, delusions, agitation (but sometimes hypoactivity), and fluctuating severity and outcomes. It can be triggered by multiple factors, including dehydration, electrolyte imbalance, upper respiratory infection, urinary tract infections, post-surgical state, and, very commonly, iatrogenic factors. Many medications, especially those with anticholinergic activity, can cause delirium in older patients. Delirium can lead to prolonged hospital stays, functional decline, cognitive impairment, and accelerated mortality.¹

So what is the evidence-based treatment for this common and serious neuropsychiatric brain disorder? None exists! Delirium is managed by identifying and addressing underlying factors, as well as supportive medical care (hydration, nutrition, sleep, monitoring vital signs, preventing aspiration, quiet rooms, orientation, and ambulation). Physical restraints are undesirable but may be hard to avoid for severely disinhibited and agitated patients who try to rip out their IV or

endotracheal tube or assault staff or family members who try to calm them during their psychotic confusional state.

Doesn't this sound similar to dementia patients in nursing homes who develop psychosis and agitation and pose management problems for their family and staff? These 2 neuropsychiatric conditions are clinically similar, and the use of antipsychotic agents is not FDA-approved for either of them. Antipsychotics have not been found efficacious for delirium² or dementia with psychosis³ but their use continues. The paradox is that C-L psychiatrists use small doses of antipsychotics routinely for delirium and generally believe that such pharmacologic intervention works in many patients, although some older agents (eg, haloperidol) have been reported to be neurotoxic⁴ and associated with higher mortality in dementia patients with psychosis.^{5,6}

The relationship of antipsychotic treatment with delirium and dementia is complex, paradoxical, and unsettled. Consider the following:

- Antipsychotics are not approved for the psychosis of dementia despite 17 large, placebo-controlled trials with 4 different second-generation agents.
- The FDA issued a "black-box" warning on all first- and second-generation antipsychotics because of a 1.6-times higher mortality rate among older patients with dementia.

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- No placebo-controlled, FDA trials of delirium have been conducted with any antipsychotic agents.

- Clinicians frequently use first- and second-generation antipsychotics for delirium despite the lack of evidence.

- The FDA has not issued a “black-box” warning on antipsychotics for use in delirium as they did for dementia, although typically both populations are older and may be susceptible to the same complications observed in Alzheimer’s disease trials (eg, strokes, transient ischemic attack, and aspiration pneumonia). This may be because of the absence of safety data of antipsychotics in delirium based on industry-sponsored registration clinical trials. No data means no warning, although the risk factors may be present for millions of older patients who have suffered from delirium and have been treated with first- or second-generation antipsychotics.

The current convoluted state of pharmacotherapy for delirium and dementia is likely to continue: dementia patients with psychosis may or may not receive antipsychotics because of the FDA’s “black-box” warning while delirium patients readily receive various antipsychotics based on long-term practice,

although not a single antipsychotic has been FDA-approved for delirium. Until a pharmaceutical company decides to conduct a large placebo-controlled trial for delirium, the current widespread, off-label use of antipsychotics in delirium will continue and “black-box” warning will apply only to 1 clinical population of older persons (those with dementia) but not another (those with delirium). Go figure!



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