

Psychosis and Agitation in Dementia: Should General Psychiatrists Care?

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Why read an article addressing whether a medication called memantine might or might not help people with Alzheimer's? Isn't Alzheimer's a rare disorder, and a diagnosis of exclusion? Isn't it just a cognitive disorder? Best addressed by others, perhaps, not us mental health types. Don't the insurance codes tell us that the only psychopathology you might see in dementia would be "with depression" or "with delusion"? (By comparison, check out the huge number of codes solely for different forms of hypertension.) Further, the U.S. Food and Drug Administration has not legitimized the treatment of psychopathology in dementia. Certainly there are more pressing public health concerns.

The article by Wilcock et al.¹ in this issue of the *Journal* has some limitations. It is a retrospective analysis of data pooled from 3 placebo-controlled studies of memantine in patients with moderate to severe Alzheimer's (I was involved with 2 of the studies). None of the studies prospectively addressed the question of relief from or prevention of psychopathology. The behavioral ratings were derived from an interview of an informant conducted by a nonclinician. The absolute mean differences found were relatively small, and the review leans on unadjusted p values to make its case. Information about the less common side effects is minimized. Some readers may find the conclusions to be somewhat overstated. The authors have financial ties to the relevant drug company. (So do I.)

But read it anyway. Notwithstanding some inherent limitations, the article is saying something useful. No, Alzheimer's and other dementias are not rare. In fact, they represent an emerging pandemic. They are readily and

specifically diagnosable. Nearly all people afflicted with Alzheimer's, the most common form of dementia, will experience some form of significant psychopathology during the course of the illness, including psychosis, depression, and agitation.² These emotional and behavioral changes are associated with serious morbidity including earlier nursing home admission, more rapid illness progression, exacerbation of functional and cognitive deficits, and increased caregiver distress. The most devastating aspects of caring for a dementia sufferer stem from accompanying behavioral problems.³ Neuropsychiatric features are cardinal elements of the illness, represent a major public health concern, and are appropriate targets for therapy.

Despite our wish that psychotropics "work" for psychopathology in dementia, the evidence from efficacy trials is weak and inconsistent. The efficacy of antipsychotics is modest for agitation associated with psychotic features as well as agitation or aggression not associated with psychosis,⁴ and effectiveness has barely been addressed.⁵ Even the atypicals are more likely to cause side effects than benefit in many cases. We are at best in equipoise for all other classes of pharmacotherapy.⁶ This leads to the hope that the modest but potentially important psychotropic effects seen in trials of antidementia agents will translate to meaningful benefit for our patients. Wilcock et al. fairly summarize what is known in this regard, and offer evidence suggesting that memantine may be beneficial for some patients, and relatively safe. We may not see many more data on the subject than these henceforth.

Now what? The limitations of pharmacotherapy underscore the sobering reality that treatment of people with dementia should begin with nonpharmacologic approaches, evaluating for possible delirium, pain, unaddressed needs, and social or environmental factors that could cause distress. Conversely, it is imperative to seek interventions that optimize the patient's residual strengths at all stages of illness.

New practice models are necessary that will allow teams of skilled clinicians the time to carefully assess and treat such complex problems and in so doing define best practice even though evidence from clinical trials is wanting. It would be ideal to combine the talents of

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medical experts working in tandem with neuropsychologists, nurses, and social workers to offer consultation to families tailored to their specific nonmedical needs. It would be better still if the patient and family also had a care manager to help implement the disease management plan. What a pity that this is not covered by insurance in the United States.

That may change, however. The United States Centers for Medicare and Medicaid Services is beginning to develop a new special needs product model for people with Alzheimer's and related dementias, a model specifically designed to address their complex health, behavioral, and social support needs. If this approach improves quality of life and is cost effective, perhaps it can be replicated nationally and lead to a new standard of care.

Millions of people, our parents and grandparents, are suffering the consequences of these deadly dementias. We do not have the evidence to define best practice, particularly for treating psychopathology. Let us make the most of the data we have, warts and all, learn from it what we

can, and move on without simply bemoaning what we don't know.

Drug name: memantine (Namenda).

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