Calming the Agitated Demented Patient

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EDITOR'S NOTE

Through this column, we hope that practitioners in general medical settings will gain a more complete knowledge of the many patients who are likely to benefit from brief psychotherapeutic interventions. A close working relationship between primary care and psychiatry can serve to enhance patient outcome.

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I (D.S.) work part-time as a psychiatrist on a palliative care team at the local Veterans Affairs hospital. In that capacity, I work alongside 3 internists who address the medical needs of our veteran population, while I focus on the psychological (emotional) side.

Some patients present problems that engage both the internist and the psychiatrist. Among them, one of the most difficult patients to treat is the individual with agitated dementia. There is no clear clinical strategy for treating dementia. There are many pharmacologic approaches offered to treat agitation.

Agitation sometimes takes the form of behavioral "acting out" (violence), which can create a situation on an inpatient unit that affects the staff as well as the other patients. The internist (or the medical resident on a geriatrics rotation) often asks the psychiatrist on the team for the best way to handle the problem this patient presents.

The atypical antipsychotic medications are sometimes employed to calm the agitated patient. Benzodiazepines are also considered as potential calming agents. In days gone by, the first-generation antipsychotic drugs (chlorpromazine, haloperidol) were typically used to quell agitation on psychiatric units and represent reasonable choices today.

One of our internists (R.P.M.) has had success utilizing a medication typically employed to treat bipolar illness: valproic acid. There is as yet no generally agreed-upon approach to the agitated, acting-out, demented patient. Dr Meyer summarizes what is known and describes her experience within the context of a patient example.

CASE PRESENTATION (DR MEYER)

Mr A is a 71-year-old man with dementia. He was admitted to the psychiatric inpatient unit for agitation and combativeness. Mr A lived in a residential care facility and had hit his roommate "with his fists and a belt." The residential care staff reported that Mr A was often combative, but that behavior control with medications generally resulted in oversedation. At the time of hospital admission, Mr A stated that "someone is trying to kill me." His conversation was otherwise illogical and impossible to follow.

During the 6 weeks of his psychiatry unit stay, Mr A was very resistant to care. His inpatient medications included haloperidol, olanzapine, escalating doses of quetiapine, and lorazepam for behavioral control. Despite these efforts, Mr A continued to have combative outbursts, alternating with medication-induced somnolence and rigidity. He was accepted on the geriatrics service for further evaluation and treatment.

At the time of his transfer to the geriatrics service, Mr A was taking quetiapine 150 mg/d and lorazepam 0.5 mg at bedtime. Valproic acid 250 mg/d was added, and quetiapine was tapered over time to 37.5 mg/d. Mr A slowly improved, although obstructiveness to care and sleep-wake confusion initially persisted. After several weeks of taking valproic acid and quetiapine, he was awake most of each day, could walk short distances with a stable gait, communicated pleasantly with staff, and was cooperative with care. When behavioral control was consistently achieved, placement was possible, and Mr A could be discharged to a nursing home.

DISCUSSION (DR MEYER)

Agitation is common in older people with dementia. Mr A's presentation and his prolonged hospitalization illustrate the struggle most providers and staff experience when faced with the agitated, combative patient with dementia. Providing reassurance and offering frequent reorientation through increased staff attention, sitters, and family may help. However, medication for behavior control is often required.

Valproic acid derivatives have been used for more than 10 years to help control agitation in dementia. This medication was originally used as an organic solvent in research laboratories until it unexpectedly showed anticonvulsant activity in a 1962 animal experiment.[1] Currently, valproic acid is a first-line antiepileptic agent. Anecdotal observations suggested that valproic acid may also have antimanic, mood-stabilizing properties, leading to successful clinical trials for the management of bipolar disorder.[1]

Early case studies of agitated dementia patients[2,3] reported behavioral improvement with decreased belligerence, hitting, and yelling and an increased willingness to cooperate with caregivers and providers. In a study published in 2007,[4] 15 demented patients with agitation were given valproic acid. Eight of these patients also received antipsychotic medication. Valproic acid alone and in combination with antipsychotic medication improved physical aggression and irritability in this study.[4]

Despite these successes in stabilizing agitated behavior, other reviews did not show such positive outcomes. A multicenter trial published in 2005 using valproic acid (divalproex is the sustained action preparation of valproic acid) as monotherapy showed "no benefit for treatment of agitation."[5(p942)] In 2009, 2 reviewers extracted information from 5 randomized, placebo-controlled trials using the Cochrane database. The reviewers found multiple flaws in the trials, but agreed with the results of the best-conducted trials that "valproate preparations are ineffective in treating agitation among demented patients."[6(p2)] However, conflicting reports have continued to emerge. In 2010, a case series examined the effectiveness and safety of using valproic acid at "low and completely flexible doses"[7(p63)] for 20 demented patients with agitation. Thirteen patients responded with improvement, and an additional 4 patients improved after adding other psychotropic medications,[7] suggesting that valproic acid may contribute to behavioral control after all. And, of course, there is Mr A, whose demeanor and behavior appeared to benefit when valproic acid was added.

Aware of these mixed findings and the resulting uncertainty for clinicians left with few effective treatments for their agitated, impaired patients, a 2012 article reviewed 20 published trials using valproic acid and its derivatives for agitated dementia.[8] The authors observed that considerable trial design differences exist among the published trials.[8] How behavior was assessed, what doses of valproic acid were used, and whether valproic acid was used as monotherapy or in combination may account for different outcomes in these trials. They concluded that "relatively low doses of valproic acid are associated with symptomatic improvement in uncontrolled trials" and that "the optimal role of valproic acid may be in combination with other psychotropics."[8(p148)] A possible synergy of valproic acid and antipsychotic medications is suggested in an animal model experiment published in 2003,[9] which reported that cortical dopamine is released to the circulation in higher levels by these medications together than by either medication alone.

Therapy with valproic acid for patients with dementia and combative behavior has a foothold in clinical care. In Mr A's history, the combination of valproic acid and quetiapine resulted in positive improvements. Flexible dosing and combination therapy may deserve more study and help agitated dementia patients and the providers caring for them.

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