Broad Approach Required in Treating Agitation, Psychosis

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SANTA FE, N.M. — Atypical antipsychotics remain the treatment of choice for the agitation and psychosis that often accompany dementia, but these agents have only modest effects, Murray A. Raskind, M.D., said at a psychiatric symposium sponsored by the University of Arizona.

A systematic approach to identifying and quantifying target symptoms—followed by an evaluation of the medical, psychiatric, and environmental contributors to the behavior—is essential, said Dr. Raskind, director of the Alzheimer's Disease Research Center at the University of Washington, Seattle.

The first step should be to gradually reduce or eliminate medications that may be exacerbating the patient's agitation or psychosis. These include theophylline and other bronchodilators, thyroid hormones, caffeine, and anticholinergics, such as antispasmodics. Withdrawal from short–half-life benzodiazepines can also result in similar symptoms.

The antipsychotics are the only drugs that have substantial evidence for efficacy in this population, and among the antipsychotics, the atypicals would be preferred because of their more favorable side-effect profiles, Dr. Raskind said at the symposium, which was also sponsored by the University of Texas, Dallas, and the University of New Mexico.

Many patients have inadequate responses to antipsychotics, however. At least two classes of drugs—anticonvulsants and antiadrenergic agents—are currently under investigation in this population and seem to show some promise.

Use of the anticonvulsant carbamazepine at a dosage of 300 mg/day, for example, was shown to be more effective than placebo in a study of 51 nursing home patients with Alzheimer's disease (Am. J. Psychiatry 1998;155:54-61). Divalproex at 800 mg/day, on the other hand, was no more effective than placebo in another study, although the investigators noted a trend in the direction of effectiveness (Am. J. Geriatr. Psychiatry 2001;9:58-66).

Dr. Raskind and his colleagues have been investigating noradrenergic function in Alzheimer's disease. Adrenergic stimulation appears to increase agitation in these patients, and propranolol—a β-adrenergic receptor antagonist—appears to be effective as an adjunct in antipsychotic nonresponders, according to an as-yet-unpublished study.

In an open-label study, prazosin, which blocks alpha$_1$ receptors, appeared to be especially effective, Dr. Raskind said. He and his colleagues tried 1-5 mg/day of prazosin on 11 nursing-home residents with Alzheimer's disease, all of whom had severe or very severe treatment-resistant disruptive agitation. After 8 weeks, the patients were judged to be moderately to markedly improved on the Clinical Global Impression scale.

Dr. Raskind has a placebo-controlled trial of prazosin under way. Meanwhile, "if you're up against the wall and you want to try something, it's helpful," he said. He cautioned that the patient should always be started at a dosage of 1 mg/day. With a higher initial dosage, there's a dramatic incidence of hypotension, which can cause a fall. This side effect disappears after several days, he said, after which the dosage may be increased gradually. ■

Atypical Antipsychotics in Dementia

	Starting Dosage (mg/day)	Maximal Dosage (mg/day)
Aripiprazole	10	20
Olanzapine	5	10
Quetiapine	25-50	400
Risperidone	0.5-1.0	2-6
Ziprasidone	20-40	80

Source: Dr. Raskind

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