

Broad Approach Required in Treating Agitation, Psychosis

BY ROBERT FINN
San Francisco Bureau

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receptor antagonist—appears to be effective as an adjunct in antipsychotic nonresponders, according to an as-yet-unpublished study.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 alpha₁ 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.

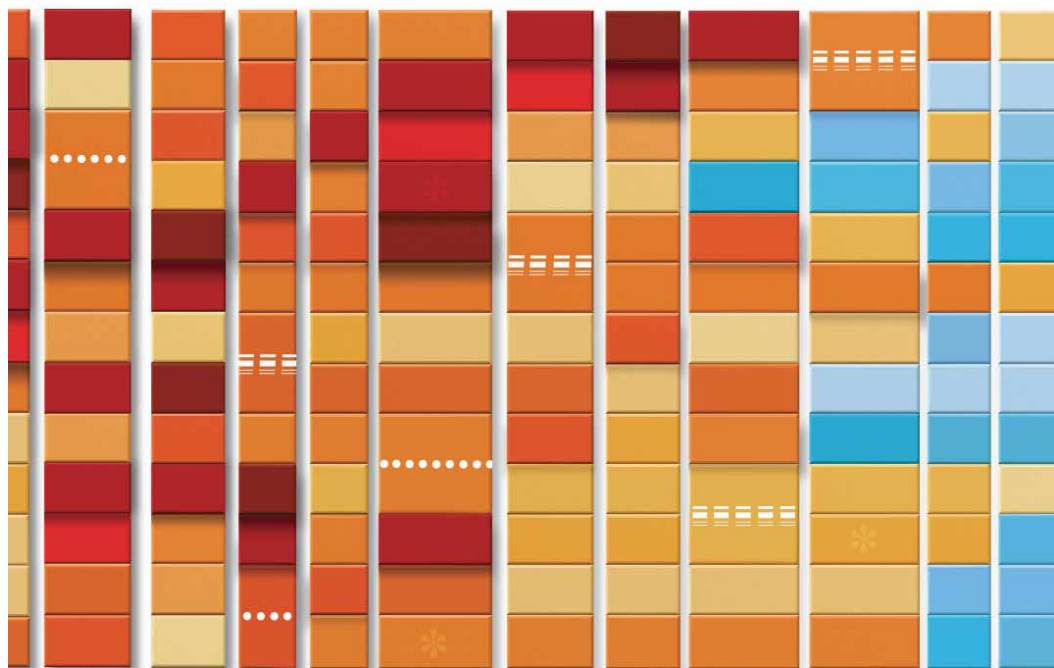
Dr. Raskind has a placebo-controlled

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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The most frequently observed adverse reactions, particularly during the initial phases of therapy, are dizziness, drowsiness, unsteadiness, nausea, and vomiting. Aplastic anemia and agranulocytosis have been reported in association with the use of carbamazepine. Reports of transient or persistent decreased platelet or white blood cell counts are not uncommon in association with the use of carbamazepine. However, the vast majority of the cases of leukopenia have not progressed to the more serious conditions of aplastic anemia or agranulocytosis. Nonetheless, complete pretreatment hematological testing should be obtained as a baseline. Discontinuation of the drug should be considered if any evidence of significant bone marrow depression develops. Because the possibility of a suicide attempt is inherent in bipolar disorder, close supervision of high-risk patients should accompany drug therapy. Equetro™ is Pregnancy Category D. Please see brief summary of Prescribing Information on the adjacent page.



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