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Combination Antipsychotic Therapy in Clinical Practice

To the Editor: Antipsychotic polypharmacy has become a fact of life in the clinical treatment of the severe psychoses. In the introduction to their article in the January issue, Tapp and colleagues (1) provide a very useful summary of the limited literature in this area. The goal of their study, which consisted of a chart review and a physician survey, was to assess providers' reasons for prescribing more than one antipsychotic medication. They correctly noted that previous studies were limited by small samples.

Tapp and colleagues chose to drop nearly half of the identified study sample, excluding 32 of 74 patients only because they were in a different division of the local Veterans Affairs health care system. Given the need for good studies in this area, this was an unfortunate decision, because it weakened the study. We need to know why clinicians in all settings are using antipsychotic polypharmacy, and dropping a significant portion of the study sample limited the utility of this study.

In addition, psychiatrists who treat psychosis particularly need to know if combining antipsychotics makes any difference in terms of clinical outcomes. Although determining physicians' rationale for prescribing combination antipsychotics is useful, the study would have been stronger if the authors had determined, from either the survey of prescribers or from the chart review, the degree of improvement among the patients who received combination therapy, perhaps using the Clinical Global Impression scale.

Finally, the decision to survey only the physicians who prescribed combination antipsychotic treatment also limited the study; it would have been equally useful to learn why these psychiatrists' colleagues did not use combination therapy and in what cases they might do so.

Because this was a community study, a report with these added elements would have more fully described the real world of management of psychosis with combinations of antipsychotic agents in a way that many public-sector clinicians, including myself, would have found valuable indeed.

George F. Parker, M.D.

Dr. Parker is associate professor of clinical psychiatry at Indiana University School of Medicine in Indianapolis.

Reference

1. Tapp A, Wood AE, Secrest L, et al: Combination antipsychotic therapy in clinical practice. *Psychiatric Services* 54:55-59, 2003

In Reply: We thank Dr. Parker for his careful review of our article and his cogent comments. He correctly notes that we surveyed clinicians at only one of the divisions of our health care system and that a larger sample may have strengthened our conclusions. However, the choice of sample should not decrease the value of the results. The results are sufficiently significant to conclude that providers continue prescribing a conventional antipsychotic in addition to an atypical

agent for two reasons: first, the provider believes that the patient's positive symptoms are responding to the combination; second, in the process of switching from one medication to another, the provider believes that the combination is the ideal pharmacologic intervention.

Dr. Parker also correctly notes that measuring the level of patients' improvement would have added useful information. Although this was not the goal of our study, it is, as we stated, important information to bring to the field. We have submitted a follow-up report with these data. However, rather than using the Clinical Global Impression scale, as Dr. Parker suggests, we used the Positive and Negative Syndrome Scale, which enabled us to determine whether positive symptoms had improved, as was suggested by the clinicians' impressions in our survey.

The value of combination antipsychotic therapy will continue to be a matter of interest for clinicians as long as we lack conclusive studies that clarify the benefits and risks of this pharmacologic intervention, and Dr. Parker is rightfully adding his opinions and questions to this debate. Far from answering all the questions that this practice raises, our study attempted to find out why clinicians proceed with long-term use of more than one of antipsychotic agent. Our study sheds some light on the rationale behind antipsychotic polypharmacy, but clearly more studies need to be conducted to assess the value of this practice.

Andre Tapp, M.D.

Dementia and Hormone Use

To the Editor: In the January issue, Baqar Husaini, Ph.D, and his colleagues (1) describe racial differences in the incidence of dementia and the costs of treating it. In their discussion, they hypothesize that relatively less common use of "hormone replacement therapy" might account for the overrepresentation

of African Americans and women with lower incomes among people afflicted with dementia.

Using similar reasoning, we believed until recently that exogenous hormones administered to peri- and postmenopausal women would prevent cardiovascular disease. Recent findings to the contrary underscore the fact that hormone users are a self-selected population whose relatively better health derives from factors more subtle than income, education, or race. Observational studies are useful for identifying areas of more systematic research but not sufficient for initiating preventive treatment of the general population.

Nada L. Stotland, M.D., M.P.H.

Dr. Stotland is professor in the departments of psychiatry and obstetrics and gynecology at Rush Medical College in Chicago.

Reference

1. Husaini BA, Sherkat DE, Moonis M, et al: Racial differences in the diagnosis of dementia and in its effects on the use and costs of health care services. *Psychiatric Services* 54:92–96, 2003

In Reply: As Dr. Stotland correctly points out, observational studies such as ours are more suited to hypothesis generation than to hypothesis testing. However, the finding that hypothesis-testing studies failed to confirm that the use of hormones lowered the risk of heart disease among peri- and postmenopausal women should not be taken as evidence that the same pertains to dementia. To give an example: observational studies suggesting a possible association between a high-fat diet and heart disease were confirmed by hypothesis testing, whereas similar associations for breast cancer were not.

Furthermore, even though observational studies are not used to generate the highest level of medical evidence, large, longitudinal observational studies are considered to produce the second-highest level of evidence and, in the absence of any class 1 evidence, can be used to gen-

erate hypotheses and guidelines. An observational study of aging from the Mayo Clinic showed that women receiving hormone replacement therapy (HRT) were less likely to develop Alzheimer's disease than women in a control group (1). These results are very similar to those of the Baltimore Longitudinal Study of Aging and other studies, which have indicated a reduction in the risk of Alzheimer's disease among women receiving HRT (2,3). These are very large longitudinal studies that have generated the same hypothesis. To the best of our knowledge, there has been no large, multicenter prospective study of HRT to either validate or negate the hypothesis. In our paper, we had only suggested the possibility that lack of HRT may be a reason for the observed disparity.

Baqar A. Husaini, Ph.D.

Majaz Moonis, M.D.

Robert Levine, M.D.

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1. Waring SC, Rocca WA, Petersen RC, et al: Postmenopausal estrogen replacement therapy and risk of AD: a population-based study. *Neurology* 52:965–970, 1999
2. Seshadri S, Beiser A, Selhub J, et al: Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *New England Journal of Medicine* 346:476–483, 2002
3. Paganini-Hill A, Henderson VW: Estrogen deficiency and risk of Alzheimer's disease in women. *American Journal of Epidemiology* 140:256–261, 1994

Outpatient Commitment: Laura's Law and the Rand Report

To the Editor: In the Law & Psychiatry column of the January 2003 issue, Paul Appelbaum provides a commentary on California's new outpatient commitment statute (1). In his analysis of the law he states, "Laura's Law begins with a preamble that recites some of the data uncovered by the Rand study [2]. Perhaps most impressive is that 37 percent of the persons involuntarily committed in California on 72-hour holds had no record of outpatient service use in the previous year. The implicit suggestion is that, had these persons been com-

pelled to accept outpatient treatment, these hospitalizations could have been avoided."

We would like to clarify that if there was indeed an "implicit suggestion," the suggestion was made by the authors of Laura's Law and not by Rand. In fact, the Rand study itself is quite clear on this point.

To quote from our letter and from our testimony in June 2002 before the California Senate Health and Human Services Committee: "We found that thousands of Californians who were sick enough to be placed in custody for evaluation of their mental condition had received no community mental health services in the year prior to their involuntary treatment. Thousands more had received only minimal outpatient treatment. The proponents of court-ordered treatment suggest that this is because people refuse treatment unless they are forced to accept it. This is an assumption based on anecdote. But a version of this same argument appears in the legislative findings of AB 1421. To be clear—while it is true that the California Department of Mental Health data do not support the assumption that use of the involuntary treatment system is caused by access problems, it is clear that the data do not support the opposite assumption either. It is just as likely that some people who want treatment cannot get it or cannot get as much treatment as they want or need. This question simply can't be answered with existing administrative data and the statement that appears in the legislative findings of AB 1421 is misleading."

Certainly the authors of Laura's Law are entitled to draw their own inferences from the data presented in the Rand report. However, the Rand report provided a balanced view, which we felt it was important to clarify for readers of *Psychiatric Services*.

I would encourage interested readers to download the report and make their own judgments about what the empirical studies, the experience of key informants in eight states, and the California administrative data say—

and do not say—about the effectiveness of involuntary outpatient treatment. The report is available on the Rand Web site at www.rand.org/icj.

M. Susan Ridgely, J.D.

Ms. Ridgely is senior policy analyst at Rand Health and Institute for Civil Justice in Santa Monica, California.

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1. Appelbaum P: Ambivalence codified: California's new outpatient commitment statute. *Psychiatric Services* 54:26–29, 2003
2. Ridgely MS, Petrila J, Borum R: The Effectiveness of Involuntary Outpatient Treatment: Empirical Evidence and the Experience of Eight States. Santa Monica, Calif, Rand, 2001

Dual Diagnosis and Treatment Compliance

To The Editor: Patients with dual diagnoses—a psychiatric disorder and a substance use disorder—have a high level of noncompliance with treatment, and they are less likely to be compliant with aftercare than patients with a single psychiatric or substance use diagnosis (1,2). Although state-of-the-art treatment for dual diagnosis patients is an integrated substance abuse–mental health treatment program (3), few urban public facilities are able to provide such extensive services. Most mental health programs have partnered with substance abuse treatment programs to provide services for these patients (4).

Engaging dual diagnosis patients in treatment remains an important goal, and the few studies addressing the process of engagement have focused mainly on patients discharged from psychiatric inpatient settings (1,2,5). Patients with dual diagnosis often obtain outpatient treatment after discharge from psychiatric emergency departments; however, compliance with aftercare in this patient group has rarely been studied. We hypothesized that compliance with outpatient mental health treatment would differ from compliance with substance abuse treatment among patients with dual diagnosis after discharge from our psychiatric emergency department.

Patients eligible for the study, which was approved by the hospital's institutional review board, were those who were evaluated in the psychiatric emergency department of a public hospital in Los Angeles County between March and August 2000. Evaluation records were reviewed, and patients were included in the study if they met criteria for a *DSM-IV* axis I psychiatric disorder as well as *DSM-IV* criteria for a substance use disorder. Aftercare plans for patients with dual diagnosis included referral to an outpatient mental health care provider or a substance abuse treatment program or both. We attempted to contact all discharged patients within 30 days after discharge. If the patient reported having attended at least one treatment session, the transition was considered successful.

Over the six-month study period, 659 of the 1,498 patients seen in the emergency department (44 percent) met criteria for a dual diagnosis. A total of 264 of the 659 patients (40 percent) had a schizophrenia spectrum disorder, 263 (40 percent) had a mood disorder, and 26 (4 percent) had an anxiety disorder. A total of 230 patients (35 percent) agreed to voluntary urine toxicology testing. Cocaine and marijuana were most frequently detected (23 patients, or 10 percent), followed by amphetamines (18 patients, or 8 percent), and opiates (five patients, or 2 percent). A total of 237 patients (36 percent) had used alcohol in the 24 hours before admission. Alcohol use was assessed by self-report or breath alcohol detection.

A total of 422 patients (64 percent) were discharged from the hospital, and we were able to contact 232 (55 percent of the discharged group) within a month after discharge. As hypothesized, patients were more likely to comply with mental health treatment than with substance abuse treatment: 102 patients (44 percent) attended at least one mental health treatment session, and 37 patients (16 percent) attended at least one substance abuse treatment session ($\chi^2=24.6$, $df=1$, $p<.001$).

In summary, we found that two-thirds of patients with dual diagnosis who were discharged from our emergency department did not comply with follow-up care. Those who received follow-up care were more likely to obtain mental health treatment than substance abuse treatment. We do not know the compliance rate among the 190 patients (55 percent of those discharged) whom we were unable to contact; however, we assume that the rate would be even lower than the rate in the contacted group. Our results confirmed that dual diagnosis patients discharged from psychiatric emergency departments have poor compliance with aftercare, especially with follow-up substance abuse treatment.

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