CATIE’s uncontrolled factors

CATIE study Phase 1 (CURRENT PSYCHIATRY, February 2006, p. 48-65) is controversial for good reason. Critical details are problematic, such as the relatively low dosage of perphenazine that might have artificially reduced tardive dyskinesia incidence among patients taking that drug.¹

A more fundamental limitation is the investigators’ use of “all-cause discontinuation” as the primary effectiveness measure. By contrast, an objective measure (Hamilton Rating Scale for Depression) was used in the STAR-D study to judge antidepressant effectiveness.

All-cause discontinuation measures are highly subjective, as patients stop taking medication for a variety of reasons:

• a spouse, parent, or friend pressured them into stopping
• they think the medication is making them weak, dependent, or vulnerable
• they don’t notice the drug’s therapeutic effects, or lack the mental skill to balance adverse and good effects
• or they are incapable of understanding that they might need to endure adverse effects to obtain a benefit.

These and other factors vary widely among patients and—in their decision process—could outweigh a medication’s objective effects on specific symptoms. These subjective factors probably obscured any objective differences among the five drugs studied in CATIE phase 1.

Other variables were uncontrolled, including:

• effects of other medications taken before and during the study. The authors state that 72% of subjects were taking other medications at baseline. Previous antipsychotics were washed out, but patients could remain on other medications. Did the investigators consider the effects of combining the study antipsychotics with these medications?

Even the washout periods seem to have been flexible (ie, not controlled) based on the study’s wording: “Overlap in the administration of (antipsychotics) that patients received before study entry was permitted for the first 4 weeks after randomization.”² In other words, some patients stayed on their previous antipsychotics for 4 weeks, and others stopped taking the previous medication sooner. Do we know enough about variations in drug metabolism and effect duration to be sure that the overlap variable did not affect the results?

• nonpharmacologic treatment. According to the study, “No care was mandated across all sites other than the drug study.”³

If other types of treatment—such as group or individual therapy—were uncontrolled across all sites, did some patients receive such care whereas others did not? If so, were the potential effects of these treatments figured into the findings?

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References:

Psychodynamic causes behind bipolar disorder, schizophrenia

The dramatic mental status changes shown by Dr. Lake’s and Dr. Hurwitz’ sample patient (CURRENT PSYCHIATRY, March 2006, p. 42-60) speak to the blurred boundaries between major illness categories in DSM-IV-TR. Discovering demonstrable brain pathology or a causative systemic medical disorder clarifies these boundaries.

continued on page 5
Dr. Randy Hillard notes that psychiatry is evolving as a specialty (CURRENT PSYCHIATRY, March 2006, p. 11), but use of atypical antipsychotics to control mood and thought symptoms accounts for much of this evolution. Bipolar disorder and schizophrenia are not biologically different mental illnesses, but rather varying abnormal manifestations of a severe mental process.

Drs. Lake and Hurwitz write that correct initial diagnosis is essential for effective psychiatric treatment. When possible, we must also consider psychodynamic causes of hallucinations, delusional behavior, or mood swings—such as unresolved conflicts and stressors—as well as the patient’s acquired insight before we can make a diagnosis.

Although psychotropics can control thought and mood symptoms, psychotherapy that delves into the psychosocial nuances at the root of the disturbance is crucial to restoring a patient with a major mental illness to sustained life activity. Unfortunately, such psychotherapy is time-consuming, and managed care restricts reimbursement for psychotherapy. In this sense, psychiatry is regressing rather than evolving.

We need to classify functional mental illnesses into major and minor entities instead of a myriad of disorders—as DSM-IV-TR has done—and focus on psychodynamic causes of psychopathology instead of speculative biological differences between mental illness presentations. This will restore sense and meaning to psychiatry as a medical discipline.

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When anticonvulsants lead to rash

The risk of serious rash leaves many psychiatrists and patients reluctant use an anticonvulsant for bipolar disorder (CURRENT PSYCHIATRY, February 2006, p. 92-100). When a minor rash develops, you must decide whether to stop the anticonvulsant and treat the allergy, or continue the offending agent lest bipolar symptoms resurface. Most physicians I know stop the anticonvulsant.

Early detection and treatment of skin problems and warning patients about the risk of rash are key to avoiding this adverse effect. I have treated the following types of rashes in patients taking anticonvulsants:

Drug rash with eosinophilia and systemic symptoms (DRESS) manifests as a delayed allergic reaction and often starts 2 weeks to 3 months after starting the anticonvulsant. It is often fatal if not detected early and treated promptly.

One patient with bipolar affective disorder, depressed type, was taking lamotrigine, 100 mg bid. She developed DRESS 7 months after starting the medication. I stopped lamotrigine and gave her diphenhydramine, 25 mg qid for 2 days, tid for 2 weeks, and bid for 1 week. The rash took approximately 4 weeks to clear.

Stevens-Johnson syndrome. A patient taking carbamazepine, 100 mg tid for bipolar affective disorder, presented with lesions of varying color, size, and shape throughout her body, including her mouth, palms, and soles. She did not have the classic “target lesion” that looks like a shooting target with several circles of varying colors. She had pain, cough, weakness, and generalized edematous joint swelling.

The patient received IV cortisone, IV fluids, antiallergic medications, and antibiotics for the skin infection. The rash subsided after 3 weeks and the skin discoloration resolved after approximately 3 months. She would not switch to lithium for fear it would sedate her but was maintained with IM fluphenazine, 37.5 mg every 4 weeks.

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