

Treating mood disorders

Russell T. Joffe, MD

Dean, New Jersey Medical School, Newark, NJ, and co-editor-in-chief, *Journal of Psychiatry & Neuroscience*

There is an emerging consensus that the goals of treatment for both unipolar and bipolar disorder have to be reassessed to include the reduction of mood disorder symptoms other than those associated with an acute episode. Until recently, the utility of any treatment for mood disorders, both unipolar and bipolar, has been judged by the rate of response to that treatment intervention, balanced by an acceptable level of side effects. For example, with acute depression, the selective serotonin reuptake inhibitors offer a significant advance over the earlier first-generation antidepressants, such as the tricyclics, in that they improved tolerability and safety without necessarily improving the antidepressant response rate. Response, however defined, usually implies a marked improvement in symptom number and severity, and it is only recently that remission versus response has become an issue, particularly in unipolar depression. Recent research efforts have focused on whether one particular class of antidepressant is more likely to induce remission than another, and claims have been made that certain antidepressants may offer more complete resolution of depressive symptoms than others. Less attention has been paid to examining and comparing the use of different treatment strategies (e.g., optimization of antidepressant dose versus combination treatment) than to which drug classes to use to achieve remission rather than response in particular patients. Moreover, the concepts of remission versus response in the various phases of bipolar illness have received little attention.

The findings of a recent study,¹ in which a cohort of patients with bipolar disorder was followed for an average of 12.8 years, are both notable and instructive. Approximately half of the time in follow-up, measured by weeks per year, was spent with depressive or manic symptoms or, in a minority of patients, with continuous cycling. Perhaps more important, of time spent ill, approximately one-quarter was spent with an actual acute clinical episode, either a major depression or acute mania. Substantially more time, roughly 3 times more, was spent either with minor syndromal illness or subsyndromal symptoms. Similar data were reported for unipolar depressed patients in a long-term follow-up by the same authors.²

The data from these studies are very clear. Acute episodes of illness, although dramatic, dangerous and substantial contributors to morbidity and mortality, tell only a small part of the story of the enormous burden of suffering that occurs with both unipolar and bipolar illnesses. Minor episodes of illness, minor depression or hypomania and, perhaps more importantly, subsyndromal manic or depressive symptoms contribute substantially to time spent ill and to the morbidity and mortality associated with these disorders.

These data are of more than passing or academic interest. They demand a refocus on the priorities for treatment for mood disorders. Acute treatment of episodes with response is a necessary but no longer a sufficient treatment goal. Rather, remission with symptom resolution should be the therapeutic goal,

Correspondence to: Dr. Russell T. Joffe, Dean, New Jersey Medical School, 185 South Orange Ave., University Heights, Newark NJ, USA 07103-2714; fax 973 972-7104; joffe@umdnj.edu

Medical subject headings: antidepressive agents; bipolar disorder; depressive disorder; remission induction; treatment outcome.

J Psychiatry Neurosci 2003;28(1):9-10.

even if it cannot be attained in all cases. Although marked symptom reduction, as achieved by the commonly used definitions of response, is highly laudable, it is not sufficient as an end point of treatment. Clinical criteria for remission need to be identified for both unipolar and bipolar disorder. Treatment studies should be designed to evaluate treatment options and their outcomes and should use definitions of remission in addition to those of response. The limited literature examining this issue in patients with unipolar depression largely compares antidepressants of one class to those of another. The data on bipolar disorder are also extremely limited — and the design of these studies presents unique methodologic challenges. The cyclic, recurrent nature of bipolar disorder, the occurrence of both manic and depressive episodes, the invariable use of multiple concurrent pharmacological strategies and the clinical and ethical issues related to medication-free periods make them particularly challenging.

Clinical lore and published research would suggest that subsyndromal symptomatology, even in the absence of acute episodes, in bipolar disorder contributes substantially to morbidity and impaired social and work function. Current mood stabilizers, including lithium and the anticonvulsants, should be evaluated

to determine not only whether they have efficacy for acute mania, acute depression and prophylaxis against acute episodes, but also whether they can induce and sustain remission and prevent long-term minor and subsyndromal depressive and manic symptoms.

Mood disorders, bipolar and unipolar, are common and cause an enormous burden of suffering. Treatment of acute episodes and, more particularly, incomplete treatment of acute episodes, address only one component of the long-term suffering of our patients. A more holistic approach is required to understand and treat the full range of clinical symptoms that contribute to the burden of suffering with these disorders. A treatment approach that aims for complete resolution of the mood disorder will serve our patients best by reducing not only their current symptoms, but also their future likelihood of recurrence.

References

1. Judd LL, Akiskal HS, Schettler PJ, Endicott J, Maser J, Solomon DA, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. *Arch Gen Psychiatry* 2002;59:530-7.
2. Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, et al. A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. *Arch Gen Psychiatry* 1998;55:694-700.

Canadian College of Neuropsychopharmacology Collège canadien de neuropsychopharmacologie

2002 Jock Cleghorn Prize

Ms. Richelle Booker is the recipient of the 2002 Canadian College of Neuropsychopharmacology (CCNP) Jock Cleghorn Prize. Ms. Booker is doing research training in the Department of Psychiatry, University of Alberta in Edmonton. This award is designed to recognize the best poster presentation by a research trainee at the Annual Meeting of the CCNP. The award, donated by the CCNP, consists of \$500. Congratulations to Ms. Booker!

Presentation: Inhibition of ^3H -GABA uptake in rat brain cortical prisms by *Hypericum perforatum*, several of its constituents and a range of commercially available preparations