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Progress in the treatment of bipolar disorder

Bipolar affective disorder has long been recognized as being one of the most significant causes of increased mortality and morbidity due to mental ill health. Bipolar disorder is an evolution of the older concept of manic-depressive illness, which itself was differentiated from dementia praecox/schizophrenia by Kraepelin over 100 years ago. Bipolar disorder was further differentiated from severe unipolar disorder following research in Europe by Angst and Perris and in the US by Winokur in the 1960s. However, unipolar and bipolar disorders are undeniably closely related, with unipolar disorder being the commonest illness in offspring of bipolar parents. Bipolar disorder has itself been subdivided into bipolar I disorder (with a history of mania) and bipolar II disorder (with a history of hypomania).

The recent “Burden of Disease” studies published in the last 10 years which have quantified the amount of years of healthy life lost to all illness show that bipolar affective disorder is one of the leading causes of increased disease burden within mental health, being roughly equal to schizophrenia (Murray and Lopez 1996).

Despite the clinical importance of bipolar disorders, they have received relatively less attention both in terms of health care funding and research than other major psychiatric disorders such as schizophrenia and major depression, which of course are themselves under-funded. This has changed somewhat recently due to the advent of novel treatments for the various phases of bipolar disorder. Lithium in its various forms has been used for over 50 years as a recognized medication for the treatment of both mania and depression, and the maintenance of wellness in bipolar disorder. However, after the introduction of lithium there was a long gap before the introduction of other novel treatments such as the anticonvulsants and atypical antipsychotics. Recently, there has been a welcome increase in the literature on the treatment of bipolar disorder. It is therefore very timely that this issue of *Neuropsychiatric Disease and Treatment* contains three review articles which bring us up to date with various developments in the treatment of bipolar disorders.

In the first review, Professor Charles Bowden and Dr Vivek Singh from the Department of Psychiatry, San Antonio, Texas, review treatment options and patient satisfaction in bipolar disorders. Charles Bowden is the principal author of many seminal works on the treatment of bipolar disorder and is particularly associated with the introduction of novel treatments, having authored landmark studies on the efficacy of drugs such as divalproex (with lithium as a comparator) and atypical antipsychotics. Professor Bowden and Dr Singh focus their research on functional recovery, which is of course the goal of treatment but has long been overlooked in the assessment of effective pharmacological treatments. They review the comparative function of individuals with both bipolar disorder and major depression and the relationship of syndromal to functional improvement, and cogently discuss efficacy versus effectiveness. They then review the various drugs from lithium through the anticonvulsants and antipsychotics with regard to their potential to alter function in patients.

The next two reviews concern atypical antipsychotics. Dr Emanuela Mundo and colleagues from Milan, Italy review the use of atypical antipsychotics “beyond psychoses”, in particular the efficacy of quetiapine in bipolar disorder. The authors note that atypical antipsychotics are successfully used in the treatment of bipolar

disorder either as adjunctive treatments or as monotherapy. They particularly focus on quetiapine, which has previously been used as a treatment in schizophrenia and is beginning to be used widely as both an antimanic and antidepressive treatment. They conclude that quetiapine is an effective agent for short- and long-term treatment of bipolar disorder, although the mechanisms of action for the various antimanic and antidepressive actions of quetiapine remain unclear. Some preliminary data suggest involvement of glutamate pathways, but the authors advise that further studies are required to clarify these issues.

The third review is by Dr Martha Sajatovic and colleagues from Case Western University in Ohio. Dr Sajatovic and colleagues note that atypical antipsychotic medications have assumed growing importance for the treatment of bipolar disorder, and that current practice guidelines in various parts of the world recommend atypical antipsychotic medication as monotherapy or as a component of polytherapy in the treatment of bipolar disorder. They then review the evidence base supporting the use of

risperidone in bipolar disorder. Most importantly, they describe dosing and administration in special populations such as geriatric, child, or adolescent patients.

These reviews are greatly to be welcomed. They consolidate and summarize much of the evidence base acquired from the last 5–10 years of research. It must be noted, however, that the only drug that has been introduced for the treatment of bipolar disorder a priori is lithium. Anticonvulsants, antipsychotics, and, indeed, antidepressants have been initially indicated and most extensively investigated in other psychiatric diseases. With the renewed interest in the treatment of bipolar disorder documented in these reviews, it is to be hoped that drug development will now focus on pharmacological treatments specific for bipolar disorder.

Reference

Murray CJ, Lopez AD. 1996. Evidence-based health policy lessons from the Global Burden of Disease Studies. *Science*, 274(5293):1593-4.