secondary to toxicity it was banned by the US FDA in 1949. In the same year in Australia John Cade published an open, small scale study which employed Lithium in the acute treatment of mania. Following this the use of Lithium spread to the UK, continental Europe (particularly Denmark where it was pioneered by Schou) and the USA. Lithium is currently used in a number of conditions. For Bipolar disorder these include acute mania and long-term prophylaxis. There has been a vigorous debate recently about the evidence supporting the use of Lithium and it is clear that whilst there is evidence to support its continuing use it is not an ideal drug. Problems include limited efficacy and side-effects including rebound mania upon sudden discontinuation. Because of these phenomena it has been suggested that prolonged treatment may be necessary to gain a new advantage from Lithium treatment. One advantage that Lithium may have over other mood-stabilisers is that it is associated with a lower suicide rate; although the pharmacological mechanism of action of Lithium is unknown it has effects on brain 5-HT function which have been suggested to be responsible for this property. However, recent work from this laboratory has shown that acute depletion of plasma tryptophan in Bipolar patients stable on long-term Lithium prophylaxis does not cause any change in suicidality ratings suggesting that Lithium's beneficial effects on suicide are not mediated via 5-HT.

Use of anticonvulsants in bipolar disorder is relatively recent and the best evidence to date is for Carbamezepine and Valproate. There have been some open studies suggesting beneficial effects from Gabapentin and Lamotrigine and full trials are underway.

Lilly-SAT2-3

OLANZAPINE VERSUS PLACEBO IN THE TREATMENT OF ACUTE MANIA

Mauricio Tohen*, Todd M. Sanger, Gary D. Tollefson. *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana 46285, USA*

A double-blind, placebo-controlled study was conducted. Patients were randomized to either olanzapine (5–20 mg/day) or placebo during a three-week period. Patients were required to be hospitalized for a minimum of one week. The primary assessment tool was the Young-Mania Rating Scale (Y-MRS), and a minimum score of 20 was required for randomization. Efficacy was measured from baseline to end point in the Y-MRS. In addition, patients were dichotomized into responders and nonresponders, where responder was defined as a 50% or greater decrease in the Y-MRS from baseline to last measurement in acute treatment.

Results: 69 patients were randomized to placebo and 70 patients were randomized to olanzapine. Olanzapine was statistically significantly superior to placebo in mean reductions of Y-MRS total (−10.3 vs −4.9, P = .09), PANSS total (−11.1 vs −3.1, P = .019), and PANSS positive scores (−4.7 vs −2.0, P = .040) from baseline to end point. In addition, there was a statistically significantly greater number of responders on olanzapine than placebo (48.6% vs 24.2%, P = .004).

Lilly-SAT2-4

THE PLACE OF ANTIPSYCHOTICS IN THE THERAPY OF BIPOLAR DISORDER

R.W. Licht. *Psychiatric Hospital in Aarhus, University of Aarhus, 8240 Risskov, Denmark*

In various parts of Europe, antipsychotics are used as first line antimanics for the majority of patients. In recent U.S. treatments guidelines for mania, lithium and antiepileptics are recommended as first line treatments, whereas antipsychotics are considered only as adjunctive agents.

Results from randomized controlled trials indicate, that typical anti-psychotics are powerful antimanics, in particular beneficial for severe agitation. As a major advantage in the treatment of these often poorly cooperating patients, no blood monitoring is required, and some typical antipsychotics can even be administered parenterally. However, the high frequency of neurological side effects from these agents may increase the risk of non-compliance, not only in the present episode but also en subsequent episodes. Moreover, due to the lack of prophylactic efficacy and due to their potential depressogenic effects, typical antipsychotics cannot be characterized as mood stabilizers. A recent placebo-controlled trial has shown that olanzapine is effective in mania with or without psychotic features. Results from uncontrolled studies also indicate that risperidone has antimanic potentials. Finally, clozapine seems efficacious in treatment resistant mania. It is beyond any doubt that the use of these atypical antipsychotics before the use of typical agents will minimize the development of neurological side effects and thereby improve compliance. However, there is still no evidence for any prophylactic efficacy of the atypical antipsychotics.

It is well-known that an antipsychotic added to an antidepressant may improve outcome in the treatment of psychotic depression, but no such data on bipolar psychotic depression are available.

In conclusion, antipsychotics are beneficial for some clinical presentations of mania. Unless parenteral administration is needed, atypical agents should be preferred before typical agents. In general, the use of antipsychotics should be prolonged into the maintenance phase only under certain circumstances.

Lilly-SAT2-5

DEPRESSION IN PSYCHOSIS AND BIPOLAR DISORDER

A. Gjerris. *Gentofte University Hospital, Denmark*

The depressive symptomatology is present in several diagnostic groups, and as such it is of interest in relation to the discussion about the relevance of the existing nosological entities and consequently in relation to choice of treatment. During the previous two decades there has been a tendency in the direction of an increasing use of polypharmacy where single symptoms such as depressive mood, aggressive behaviour and anxiety are treated specifically, although they occur in the context of an otherwise well defined nosological entity for which we think we to have a specific treatment. In relation to schizophrenia we are discussing the existence of postpsychotic depression, depression related to the acute schizophrenic symptomatology and to akinesia and psychogenic depression. In affective disorder we are discussing whether there is a clinical difference between bipolar and unipolar depression with regard to symptomatology, course and epidemiology and whether the depressive state under these two conditions should be treated differently. Moreover the problems occurring in treating mixed states of mania and depression are in focus. The challenge in the future is to develop treatment modalities, which have a positive effect on all elements of a disorder - including depressive symptoms - in a specific diagnostic group, or, if this is not possible, to develop treatment programs based on polypharmacy. Finally it maybe relevant to reevaluate whether the existing diagnostic classification is meaningful in relation to choice of treatment.