Adjunctive use of olanzapine in the treatment of mania

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Olanzapine is an atypical antipsychotic which is licensed only for the treatment of schizophrenia. Two cases are described in which olanzapine was used as an adjunct to lithium in treating mania in patients with bipolar disorder. In both cases the lithium-olanzapine combination was more effective and better tolerated than a previous combination of lithium with a traditional antipsychotic. Olanzapine may offer significant advantages over traditional antipsychotics in the treatment of mania, but controlled trials are needed to confirm this. (Int J Psych Clin Pract 1999; 3: 213–215)

Keywords
bipolar disorder *mania*
atypical antipsychotics *compliance*

INTRODUCTION

Olanzapine is an atypical antipsychotic licensed only for the treatment of schizophrenia.[1] To date no trials have been published which compare its efficacy with that of a traditional antipsychotic in the treatment of mania. However, in a 3-week double-blind placebo-controlled trial of patients with mania, olanzapine was statistically significantly superior to placebo in mean reductions on the Young-Mania Rating Scale.[2] A secondary analysis confirmed its superiority to placebo in patients with rapid-cycling bipolar disorder.[3] A small number of case reports also suggest it is effective when used alone in the treatment of mania[4,5] and when used as an adjunct to mood stabilizers in the treatment of mania[5,6] and mixed mood states.[7] In contrast to these favourable reports, in one single case report[8] olanzapine appeared to cause mania in a patient with no previous history of mania.

We have successfully used olanzapine to treat several patients with mania. We report two such cases and discuss the implications. As far as we are aware, these are the only case reports of olanzapine being used in combination with lithium to treat mania; previous reports of olanzapine in mania[5,6] have involved other mood stabilizers such as valproate or lamotrigine.

CASE 1

A 35-year-old caucasian man was admitted under the 1983 known patient with bipolar affective disorder, who had had his first episode at the age of 25 years. Several previous manic episodes had resulted in compulsory admissions. On this admission he was overactive, disinhibited and showed aggressive behaviour. His mood was irritable and elated, his speech showed flight of ideas, he had grandiose delusions, his sleep was disturbed and his concentration was poor. A urinary drug screen revealed no illicit substances. Prior to admission he had been controlled on lithium alone; a serum lithium estimation 6 days before admission, when he was mildly hypomanic, was within the therapeutic range (12-h level: 0.8 mmol/l). Consequently it was felt that the current episode could not be attributed to poor compliance with lithium treatment. Following admission lithium was continued and haloperidol started. This was rapidly titrated up to 10 mg bd. He showed some improvement but continued to be overactive, with pressure of speech and disturbed sleep, and he also developed akathisia. After 6 weeks the haloperidol was replaced with olanzapine 10 mg od. Within one week of commencing olanzapine the akathisia and the residual manic symptoms had resolved. Since discharge he has remained in remission on olanzapine and lithium.

CASE 2

A 23-year-old Asian man was admitted informally with a manic illness. He was a known patient with bipolar

of 20 years. On admission he showed overactive and disinhibited behaviour, and his mood was irritable and elated, with pressure of speech, grandiose delusions, disturbed sleep and poor concentration. A urinary drug screen revealed no illicit substances. Until admission he had been controlled on 1 g lithium daily. His relapse appeared to be secondary to poor treatment compliance. He was commenced on thioridazine 100 mg tds in addition to continuing with lithium. Within a few days he complained of impotence and delayed ejaculation. Four weeks later his sexual dysfunction was continuing to cause him distress and there was only a minor improvement in his mental state, despite his serum lithium being within the therapeutic range. Consequently his thioridazine was stopped and olanzapine was commenced at 10 mg od and then increased to 15 mg od. Over the next 4 weeks, his manic symptoms totally resolved and his sexual function returned to normal. Since discharge he has remained well on olanzapine and lithium.

DISCUSSION

In both cases a manic illness, resistant to 4–6 weeks' inpatient treatment with lithium at therapeutic plasma levels plus a conventional antipsychotic, responded after the antipsychotic was changed to olanzapine. The possibility that recovery was due to another factor and only coincidental to starting olanzapine must be considered, but it appears unlikely. For example, in both patients a drug screen on admission was negative, ruling out a drug-induced psychosis in which abstinence would have accounted for recovery. The time course of recovery, 4–6 weeks after admission, also goes against this hypothesis. In case 2, the manic episode appeared secondary to poor compliance with lithium. Consequently it could be argued that recovery marked the onset of the antimanic action of lithium which was restarted on admission. In case 1 the therapeutic serum lithium 6 days before admission, when the patient was already hypomanic, rules out lithium non-compliance as a cause of the illness. Consequently recovery cannot be attributed to lithium alone and the argument that olanzapine was responsible is particularly strong. In both cases there was no evidence of any adverse interaction between olanzapine and lithium.

An important observation is that with traditional antipsychotics both patients showed disabling side-effects (case 1, akathisia; case 2, sexual dysfunction) which resolved when olanzapine was commenced. A low incidence of extrapyramidal side-effects and sexual dysfunction has been demonstrated in double-blind trials of olanzapine.[9] The improved tolerability of atypical antipsychotics is important, not only to improve the quality of life, but also because patients may be more compliant with treatment. Poor compliance is a major factor in causing relapse in patients with bipolar affective disorder. Tardive dyskinesia is a delayed but frequent complication of treatment with conventional antipsychotics, particularly in patients with bipolar affective disorder,[10] and this is a further reason to consider an atypical agent when long-term antipsychotic treatment is required. Although our two patients did not experience significant side-effects with olanzapine, it must be stressed that atypical antipsychotics do have side-effects, though these are generally less numerous and troublesome than those found with conventional agents.

Anecdotal reports must be viewed with caution. The main disadvantage of using olanzapine to treat mania is the lack of supporting data from randomized double-blind trials comparing it with accepted treatments such as haloperidol. This is particularly important in view of a recent case report[8] in which olanzapine may have induced mania. Furthermore, reports on the mood-altering effects of risperidone, a novel antipsychotic with some pharmacodynamic similarities to olanzapine, are conflicting. Reports of its effectiveness in treating mania[11] are countered by reports of cases in which it appeared to induce or exacerbate mania.[12,13]

Another disadvantage of atypical agents is their higher cost, though in the long term this could be offset by improved compliance and a reduced relapse rate.

In summary, we recommend that, for the present, when an antipsychotic is required in the treatment of mania, conventional agents should remain the first choice. However, if problems arise due to poor tolerability or lack of efficacy, one should consider olanzapine where preliminary data supports its efficacy. Controlled studies are needed to confirm these initial impressions.

KEY POINTS

- Antipsychotic side-effects contribute to poor compliance and relapse in bipolar disorder
- Preliminary data suggest that olanzapine is effective and well tolerated in treating mania, alone or as an adjunct to mood stabilizers
- Controlled trials are needed to confirm this
- Currently conventional agents remain the antipsychotics of choice in mania
- If problems arise due to poor tolerability or lack of efficacy, olanzapine should be considered

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