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Lamotrigine in the Treatment of Schizoaffective Disorder

Key Words
Lamotrigine
Schizoaffective disorder
Bipolar disorder
Rapid cycling
Serotonin

Abstract
There is accumulating evidence for the efficacy of lamotrigine in the treatment of bipolar disorder, including bipolar depression, both as monotherapy and in combination with sodium valproate. We present the cases of 3 female patients admitted to our hospital with the diagnosis of schizoaffective disorder who were treated with lamotrigine. While dosages up to 200 mg/day, resulting in serum concentrations of less than 5 mg/l, were only partially effective, 400 mg/day (with serum concentrations >10 mg/l) led to considerable mood stability, with complete remission from paranoid symptoms. We suggest that lamotrigine might be helpful in the treatment of schizoaffective disorder, probably with serum concentrations of more than 5 mg/l.

Recently, considerable evidence has accumulated that lamotrigine is effective in the treatment of bipolar disorder, both as monotherapy [1] and in combination with valproate [2], a drug known to markedly increase blood levels of lamotrigine [3]. In particular, lamotrigine might be helpful in treatment-refractory bipolar disorder [4–6], rapid-cycling bipolar disorder [7, 8], bipolar depression [9–11] and bipolar mania [12].

Here we report on 3 female patients admitted to the Munich University Psychiatric Hospital with the diagnosis of schizoaffective disorder who were consecutively treated with lamotrigine as monotherapy. All patients had experienced numerous episodes in the past and were not responsive to lithium and/or did not tolerate sodium valproate. Depressive episodes in the past had frequently required use of antidepressants with the consecutive risk to induce a new schizomanic episode.

Case Reports

Case 1

This 33-year-old bank clerk was admitted 9/97 with a severe schizomanic episode. She was previously diagnosed as schizoaffective disorder, having 6 schizomanic episodes since age 21, with full remission in between. Originally, the disorder started with a severe depression and a suicide attempt in 1986. The patient continuously took lithium since 1993, the last schizomanic episodes were 3/97 and 9/97. Lithium was discontinued because of the lack of efficacy, hypothyroidism and weight gain. The acute schizomanic episode was treated successfully with a sodium valproate loading therapy. After discharge 12/97, the patient developed a severe loss of hair and lamotrigine was introduced with the aim of substituting for sodium valproate. Lamotrigine was well tolerated and in 2/98 a serum concentration of 4.8 mg/l was reached with 125 mg of Lamictal®. At this point, the patient developed a light manic episode without paranoid symptoms which led to admission to our hospital; it was important for the patient that this was the first time she was not admitted against her will. Manic symptoms were considerably diminished by further increasing lamotrigine serum concentrations (9.3 mg/l, administration of 400 mg Lamictal).

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Case 2

Mrs. L. is a 31-year-old opera singer who was admitted to our hospital in 11/97 with the diagnosis of schizomanic episode. In the past 10 years at least 3 depressive and 2 manic episodes were observed with full remission in between, at this time she also exhibited severe thought disorder, delusions and hallucinations leading to a ICD-10 diagnosis of schizomanic episode. The patient, who is a lithium nonresponder, received lamotrigine. Termination of the schizomanic episode was achieved with dosing up to 300 mg/day Lamictal, leading to a serum concentration of 7.7 mg/l. After discharge a very light depression was observed, no antidepressant medication was necessary.

Case 3

The 37-year-old cosmetician was admitted in 6/97 with a severe schizomanic episode. Since 1979 the patient was admitted at least 40 times in different psychiatric hospitals because of mania, severe depression or schizomania. In the last 3 years no full remission was achieved as a rapid cycling between (schizo)mania and depression had to be observed despite several therapeutic attempts to influence the disease. Lithium was not able to prevent severe manic episodes, carbamazepine was equally ineffective and sodium valproate led to hair loss. The episode in 6/97 was treatment-resistant to high doses of flupentixol as well as to 25 mg of olanzapine. A therapy with lamotrigine was started and discharge was possible in 8/97. Unfortunately, in 12/97 depression and severe suicidal thoughts developed despite 200 mg of Lamictal monotherapy (serum concentration of 2.4 mg/l), consecutively lamotrigine was combined with 150 mg of venlafaxine. This strategy led to induction of a new schizomanic episode. At this point, venlafaxine was discontinued and cis-clopentixol added to lamotrigine. In 1/98 discharge was possible, the last serum concentration of lamotrigine was 5.1 mg/ml (400 mg Lamictal). Cis-clopentixol was discontinued. In 3/98 a light depression without suicidal thoughts was observed, no antidepressant drug was prescribed at this point.

Discussion

The history of these patients shows that lamotrigine can be used safely and successfully in treatment-resistant schizoaffective disorder. Because of the risk of skin rashes lamotrigine – unlike sodium valproate – cannot be given as a loading therapy. Our cases suggest that, unless serum concentrations of more than 5 mg/l are reached, lamotrigine does not seem to display its full protective action. It might be useful to initially combine lamotrigine with other potentially efficacious substances. Once dosed up to approximately 400 mg/day, lamotrigine in our patients seemed to be effective in a variety of schizoaffective symptoms as paranoid symptoms, hallucinations, thought disorder, manic and depressive symptoms. The efficacy of lamotrigine in treating the schizophrenic component parallels the reduction of ketamine effects in healthy humans reported by Anand et al. [13] and might be mediated by reduction of glutamate release. The efficacy of lamotrigine in reducing depressive symptoms might be linked to 5-HT uptake inhibition, an effect described in both rat and human tissue by Southam et al. [14].

In summary, further studies and long-term observation of the effects of high doses of lamotrigine are necessary; because of its dual action on both glutamate and 5-HT neurotransmission, lamotrigine might be particularly useful in the treatment of schizoaffective disorder.

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