Manic Episode Associated with an Abrupt Shift from Sulpiride to Quetiapine in a Young Man with Schizophrenia

Chien-Liang Lai, M.D., Hung-Yu Chan, M.D., Hsiao-J u Sun, M.D.

**Introduction:** We report a case of manic episode associated with an abrupt shift from sulpiride to quetiapine in a young man with schizophrenia. **Case report:** This 20-year-old schizophrenic male had persistent psychotic despite sulpiride 2000 mg/d treatment. Extrapyramidal symptoms were noted after sulpiride was administrated for one week. Sulpiride was abruptly discontinued and replaced by quetiapine, which was titrated to 600 mg/d on the 6th day after starting quetiapine. On the 7th day after starting quetiapine, manic symptoms were noted with a Young Mania Rating Scale score of 25 and a Positive and Negative Syndrome Scale score on the positive scales of 19. Quetiapine was discontinued and replaced by haloperidol 10 mg/d two weeks after the onset of manic symptoms. Two weeks after switching to haloperidol, the manic symptoms remitted completely. There was no recurrence of manic symptoms during 21 months follow up. **Discussion:** Quetiapine has relatively lower potency on D2 receptors blockade compared to other atypical antipsychotics. The anti-serotonergic effect of atypical antipsychotics might induce dopamine secretion. Inadequate suppression D2 receptors might increase the likelihood of manic symptoms. The abrupt switch from sulpiride to quetiapine in this patient may also have resulted in a rebounding of dopaminergic activity, which might have contributed to the development of manic symptoms.

**Key words:** Quetiapine, atypical antipsychotic, manic episode, D2 receptors

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ed the treatment of olanzapine, risperidone, quetiapine, zipasidone and aripiprazole for acute manic symptoms. However, a review by Aubry et al. revealed that olanzapine and risperidone might induce manic or hypomanic symptoms [1]. Ziprasidone has also been reported to have an association with the development of manic or hypomanic symptoms [2]. Our review of the literature found only one report about quetiapine-inducing manic symptoms and two reports with hypomanic symptoms [3-5]. Two of these reports did not regularly assess manic and psychotic symptoms with rating scales during the manic episodes [3,4] and another had a short period of follow up [5]. We report a case of manic episode which developed after abrupt shifting from sulpiride to quetiapine and discuss its possible pathogenesis.

**Case report**

This 20-year-old male had a three-year history of psychotic symptoms. Initial presentation and behavioral symptoms included functional impairment, social withdrawal, auditory hallucination, reference delusion, and persecutory delusion. He claimed that he had heard ghosts' voice and they had tried to persecute him. He had no past history or family history of affective symptoms, and no history of head injury or substance use. Diagnosis of paranoid schizophrenia was made but he didn't receive medication treatment until cis-clopalenthixol 25 mg/d was prescribed at the second visit. Compliance with this treatment was irregular and he was admitted to the acute psychiatric ward about one month after his first outpatient visit. Sulpiride was administered starting on the first day of admission with an initial dosage of 600 mg/d. The dosage was gradually titrated to 1000 mg/d from the second week and up to 2000 mg/d at the beginning of the fourth week of admission. Acute dystonia and parkinsonism were also noted since the second week of admission. Trihexyphenidyl 5-10 mg/d, clonazepam 1.5 mg/d and flurazepam 30-60 mg/d were also prescribed for EPS and the symptom of insomnia. Despite maintaining sulpiride at over 1000 mg/d for four weeks, his psychotic symptoms persisted with severe EPS. Therefore, sulpiride was replaced by quetiapine abruptly. The initial dosage of quetiapine was 100 mg/d and was stepped up by 100 mg increments each day until reaching 600 mg/d. On the 7th day after starting quetiapine, manic symptoms developed with elated mood, talkativeness, hyperactivity, colorful dressing and grandiose delusions. The contents of grandiose delusions were manifested as his being the God, becoming Michael Jordan's teacher and being an actor's son. Reference and persecutory delusions also persisted with the same contents. Manic and psychotic symptoms were assessed weekly using the Young Mania Rating Scale (YMRS) and positive scales of the Positive and Negative Syndrome Scale (PANSS). Initial scores on the YMRS and the positive scales of the PANSS were 25 and 19, respectively. Laboratory workup performed during the manic episode including complete blood count with white cell differential, blood chemistries and thyroid function tests revealed no abnormalities. Due to persistence of the manic symptoms, quetiapine was switched to haloperidol 10 mg/d at the eighth week of admission. Two weeks after switching to haloperidol, his psychotic symptoms remained the same but affective symptoms remitted completely. The patient's psychotic symptoms improved and he was discharged during the eleventh week of hospitalization. At discharge, YMRS total score was 0 and the score of the positive scale of the PANSS at discharge was 12 (Figure 1). Regular treatment with haloperidol was given during the following 21 months with
Figure 1. Drugs dosages, scores of YMRS and PANSS-P during admission

The dose tapered to 5 mg/d in the fourth month after discharge. His manic symptoms did not recur and psychotic symptoms remained stable during this period. At last follow up after discharge, the positive scale score of the PANSS was 8 and he continued to show functional impairment and negative symptoms of avolition and anhedonia.

Discussion

The manic symptoms of this young male patient occurred one week after an abrupt switch from sulpiride to quetiapine, and significantly improved after switching from quetiapine to haloperidol. No overt evidence of affective symptoms
were noted during a follow up period of 21 months with continuing haloperidol treatment. This patient had no personal or family history of affective disorder. Differential diagnosis of schizoaffective disorder with superimposed manic episode during the course of psychosis could not be made due to the temporary nature within the disease course. The occurrence of manic symptoms may have resulted from the abrupt discontinuation of sulpiride and the resolution of symptoms may have been due to the administration of haloperidol. We were unable to definitively establish that the manic symptoms were due to the use of quetiapine.

One of the possible mechanisms by which atypical antipsychotics may induce manic episodes is the reduction in the suppression of dopamine from serotonin and enhanced the secretion of dopamine over the forebrain area due to the relatively higher 5-HT2 receptors blockade of atypical antipsychotics [6]. Quetiapine also has a relatively lower potency for D2 receptors blockade than other atypical antipsychotics [7] and the dopamine secretion might therefore be large and inadequately suppressed by serotonin leading to the onset of manic symptoms.

Sulpiride-associated prolactinemia and body weight gain may influence the development in teenagers. The National Health Insurance system instituted special regulation for the usage of atypical antipsychotics three years ago, so we chose sulpiride as his initial medication. It is possible abrupt switch from sulpiride to quetiapine due to unsatisfactory treatment response and severe EPS may have resulted in a sudden decrease in D2 receptors blockade, and that rebounding dopaminergic activity could have induced manic symptoms. Due to the potential impact of abrupt discontinuation of sulpiride, cross-titration or overlap and tapering of sulpiride might be suggested in order to prevent manic symptoms [8].

Our review of the recent literature from large clinical trails of atypical antipsychotics revealed no association between manic or hypomanic episodes and the use of atypical antipsychotics [9,10]. However, case reports of atypical antipsychotics inducing manic or hypomanic symptoms have been reported [3-5]. Clinicians should take precautions to prevent and manage possible atypical antipsychotic-associated manic episodes. However, the risk factors for development of manic symptoms while using atypical antipsychotics remain to be determined.

The results of this case and our review of the literature suggest the following as possible conclusions: 1) quetiapine-associated manic symptoms may be related to its relatively lower potency for D2 receptors blockade and higher potency for 5-HT2 receptors blockade; 2) abrupt switching to quetiapine from sulpiride may induce rebound dopaminergic activity leading to manic symptoms; 3) the use of cross-titration when switching antipsychotics may reduce the risk of manic symptoms.

References

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