Clinical Case Study

TREATMENT OF DEPRESSIVE MOOD IN SCHIZOPHRENIA WITH THE ATYPICAL ANTIPSYCHOTIC QUETIAPINE

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Two patients with schizophrenia and depressive mood experienced remission in both their psychotic and depressive symptoms during treatment with the atypical antipsychotic quetiapine. These case reports illustrate the antipsychotic clinical efficacy of quetiapine and its antidepressant effects in the treatment of patients with schizophrenia and depressive mood. Depression and Anxiety 11:80–82, 2000. *Published 2000 Wiley-Liss, Inc.*[†]

Key words: *quetiapine; schizophrenia; antipsychotics; depression; treatment*

INTRODUCTION

Depressive mood during the course of schizophrenia had been commonly reported in the literature [Birchwood et al., 1993; Tollefson et al., 1998]. Between 20% to 40% of patients with schizophrenia who manifest depressive symptoms have been reported to attempt suicide [Meltzer and Okayli, 1995]. In this report two patients with schizophrenia who manifested depressive symptoms and suicidal ideation had remission of their depression during treatment with quetiapine, an atypical antipsychotic medication.

CASE REPORTS

CASE I

Mr. A., a 32-year-old single Caucasian male veteran, presented with the chief complaint of sadness and loss of interest in all pleasurable activities. These symptoms had lasted for 2 weeks and met the DSM-IV diagnostic criteria for a depressive disorder not otherwise specified [American Psychiatric Association, 1994]. He had a history of psychotic symptoms, which met DSM-IV diagnostic criteria for chronic paranoid schizophrenia [American Psychiatric Association, 1994] and had received prior treatments with chlorpromazine, haloperidol. and thiothixene. He discontinued these medications because apparently they aggravated his depressed mood. Mr. A. never abused alcohol, illicit drugs, tobacco, or caffeine. Mr. A. had a 2 week course of treatment with clozapine, which resulted in remission of both his psychotic and depressive symptoms. Clozapine was discontinued due to the development of agranulocytosis. Mr. A. had been off clozapine for 3 weeks; he worried about the recurrence of auditory hallucinations, persecutory delusions, and suicidal intention. He had attempted suicide once in the past by pesticide overdose. Mr. A. consented to treatment with the atypical antipsychotic quetiapine. He also agreed to comply with daily outpatient monitoring.

Treatment began with quetiapine 25 mg a day, which was increased, by 25 mg every third day until a dose of 50 mg three times daily was reached. On the 18th day of treatment, Mr. A. developed somnolence. The quetiapine dose was changed to 150 mg at bedtime. On the 24th day of treatment, the somnolence subsided and although the psychotic symptoms of hallucinations and delusions remained in remission, the depressive symptoms of hopelessness, worthlessness, decreased energy, decreased concentration, and suicidal ideations persisted. Quetiapine dose was increased to 200 mg at bedtime. On the 36th day of treatment, Mr. A. reported complete resolution of his depressive symptoms and he had no adverse effects to quetiapine.

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It has now been 6 months since the treatment of quetiapine was initiated and Mr. A. continues to comply with his 200 mg bedtime dose. He has not had any recurrence of schizophrenia associated psychotic or depressive symptoms. He has been able to work on a part time basis in a grocery store and also joined a church. He has not developed any side effects to quetiapine and wants to be maintained on it permanently.

CASE II

Mr. B., a 43-year-old black single male veteran, presented with a complaint of depression that began 3 months following a heavy storm, which destroyed most of his rented house. Although he denied current suicidal ideation, he described early morning awakening, feelings of guilt, and inability to enjoy any pleasurable activities. Owing to the duration and severity of these symptoms, he met the DSM-IV diagnosis of a depressive disorder not otherwise specified [American Psychiatric Association, 1994]. Mr. B. had a 15 year documented history of psychotic symptoms, which met the DSM-IV diagnostic criteria of chronic disorganized schizophrenia [American Psychiatric Association, 1994]. He has not abused any alcohol, illicit drugs, or caffeine for 8 years but smoked one pack of cigarettes a day for the last 5 years.

Mr. B. was non-compliant with haloperidol decanoate treatment and although he denied current hallucinations, he had beliefs that were delusional in nature. In the past, Mr. B. had responded to command hallucinations and had inflicted superficial burns on both his upper and lower extremities. Mr. B. acknowledged that he wished to die because he could not bear the deep and severe feelings of depression. He agreed to be hospitalized for safety and initiation of treatment.

Treatment started with quetiapine 150 mg daily and increased weekly by 150 mg until a dose of 150 mg three times a day was reached. Toward the end of his third week of treatment, he noticed a marked improvement in his way of thinking; his delusions about being punished by God subsided. He developed a mild headache, which was well tolerated. In order to enhance compliance, quetiapine dose was changed to 450 mg at bedtime. Despite the resolution of the psychotic symptoms, Mr. B. was still experiencing depressive symptoms of early morning awakening and inability to enjoy pleasurable activities. He felt safe to be discharged to weekly outpatient treatment. Quetiapine dose was raised to 500 mg at bedtime. Within 8 weeks of initiation of quetiapine treatment, the mild headache subsided and the depressive symptoms remitted.

Mr. B. continued to do well on quetiapine, and for the past 5 months he has not experienced any exacerbation of psychotic or depressive symptoms. He has complied with the 500 mg bedtime dose as well as a bi-weekly out patient follow-up.

DISCUSSION

Although traditionally mood disorders were viewed as distinctly separate from schizophrenia [McGlasham and Carpenter, 1976], recent findings highlight that depressive symptoms are common in schizophrenia and often severe and are associated with higher rates of relapse [Birchwood et al., 1993] and of suicide [Roy, et al., 1993]. Siris [1995] also noted the common occurrence of depressive symptoms in schizophrenia during the first episode of psychosis. The range of depressive symptoms had been estimated to be from 7 to 65%, with a modal rate of 25% [Hirsch and Jolley, 1989; Johnson 1988; Koreen et al., 1993]. The diagnosis of depression in patients with schizophrenia is included under the of DSM-IV category of depressive disorder not otherwise specified [American Psychiatric Association, 1994]. The American Psychiatric Association (APA) and the Expert Consensus Group have published guidelines advising clinicians to consider the diagnosis and treatment of post psychotic depression in schizophrenia [Smith and Docherty, 1998].

Tollefson et al. [1998] pointed out that despite the prevalence, the severity, the psychosocial complications, and the prognostic value of depressive symptoms in schizophrenia, there are relatively few treatment studies addressing this clinical topic in the literature.

Prior to the advance of atypical antipsychotics, combination of antipsychotics and antidepressants was used in the treatment of depressive and psychotic symptoms [Azorin, 1995]. The addition of antidepressants however could lead to exacerbation of psychotic symptoms [Smith and Docherty, 1998]. In a multicenter clinical trial, [Müller-Siecheneder et al., 1998] compared risperidone with a combination of haloperidol and amitriptyline in patients with coexisting psychotic and depressive symptoms, and found risperidone to be no better than the haloperidol amitriptyline combination.

Hillert et al. [1992] observed a "clinically significant improvement of depressive symptoms" in ten patients with schizophrenia treated with risperidone. In a population of 421 patients with schizophrenia and suicidal ideation; treatment with the antipsychotic clozapine lead to marked decrease in suicidalilty during a follow-up period of 6 months to 7 years [Meltzer and Okayli, 1995]. In a prospective blinded trial conducted in 17 countries with 1996 patients, depressive signs and symptoms in schizophrenia responded to treatment with olanzapine [Tollefson et al., 1998]. At the time of writing this report, there are no published reports on the effectiveness of quetiapine in treating depressive symptoms, which prompted the reporting of these two cases.

The atypical antipsychotic medications clozapine, risperidone, olanzapine, quetiapine, and others in addition to their effectiveness in treating the positive symptoms of schizophrenia are effective in treating negative symptoms that are difficult to differentiate from depressive symptoms. They also possess a low potential of causing extrapyramidal side effects (EPS). EPS may

contribute to or mimic the psychomotor retardation symptoms of depression [Tollefson et al., 1998].

Quetiapine (Seroquel) is a dibenzothiazepine with affinity for $5HT_2$, H_1,α_1, -and α_2 -adrenegic receptors with minimal affinity for dopmamine D_1 receptors. Although it resembles clozapine in its pharmacologic profile, quetiapine lacks appreciable affinity for muscarinic cholinergic and benzodiazapine binding sites [Saller, 1993]. Both $5HT_2$ and D_2 neuro transmission have been implicated in mood disturbances [Hyman, 1995]. Since quetiapine pharmacological activity is related to these receptors, it could be an appropriate agent to investigate in clinical trials for its effects on depressed mood in schizophrenia.

In summary these two case studies illustrate the possibility of using the atypical antipsychotic quetiapine for the treatment of depressive symptoms in schizophrenia. It could be argued that the remission of the depressive symptoms was not attributed to the atypical antipsychotic quetiapine but rather incidental or due to the passage of time. Without conducting larger well-designed placebo-controlled randomized trials to evaluate the effectiveness of quetiapine on treating both psychotic and depressive symptoms in schizophrenia the clinical outcome in these two cases represent only interesting clinical observations.

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