

## OBSESSIVE - COMPULSIVE SYMPTOMS DURING CLOZAPINE TREATMENT

A.K. AGARWAL & ABDUL KHALID

### ABSTRACT

*Development of obsessive-compulsive symptoms during clozapine treatment in schizophrenics has been noted in few reports from west. In our cases, three schizophrenic patients resistant to typical antipsychotics developed obsessive-compulsive symptoms during clozapine treatment. Since clozapine is a potent 5-HT<sub>2</sub> receptor blocker, role of serotonergic systems in the development of obsessive-compulsive symptoms may be considered. It may be prudent to be vigilant for the emergence of obsessive-compulsive symptoms in all patients treated with clozapine.*

**Key words :** Clozapine, obsessive-compulsive symptoms, schizophrenia

Major adverse effects associated with clozapine treatment are sedation, tachycardia, constipation, dizziness, hypotension, hyperthermia, sialorrhoea, seizures and agranulocytosis (Kammen & Marder, 1995) but there are occasional reports of development of obsessive-compulsive symptoms during clozapine treatment in schizophrenic patients (Patel, 1992; Cassady & Thaker, 1992; Patel & Tandon, 1993). In a short span of two years, out of nearly hundred patients treated with clozapine, we encountered three schizophrenic patients who developed obsessive-compulsive symptoms.

### CASE -1

Ms. A, a 20 year old girl with treatment refractory paranoid schizophrenia, responded well to treatment with clozapine (300 mg/day) with improvement of both positive and negative symptoms. After four months of treatment with clozapine, she developed obsessive-compulsive symptoms, predominantly compulsive in form of repetitive checking and cleaning rituals. It was decided

not to discontinue clozapine as her schizophrenic symptoms, which were in remission with clozapine, had not responded to adequate trials of typical antipsychotics and even risperidone in the past and obsessive-compulsive symptoms were not severe enough to hamper her day to day functioning.

### CASE- 2

Mr. B, a 32 year old man was suffering from paranoid schizophrenia from the age of 20 year and was resistant to various traditional antipsychotics. He was placed on clozapine and his dosage gradually increased to 450 mg/day to which he responded. When the dosage was reduced to 400 mg/day, the patient developed obsessive doubts which he described as repetitive, intrusive, irrational, and caused marked anxiety. On reverting to earlier dosage (450 mg/day) his obsessive doubts partially ameliorated. However, he still experiences obsessive doubts but prefers them to reduced-dosage of clozapine because he feels

that he was never as good earlier.

### CASE- 3

Mr. C, a 32 year old man diagnosed as a case of paranoid schizophrenia for six years was treatment resistant. Clozapine was started and gradually increased to 400 mg/day. After one year of treatment he developed severe obsessive-compulsive symptoms due to which clozapine had to be stopped and he was given tablet trifluoperazine (7.5 mg/day). Interestingly, his resistant schizophrenic symptoms responded to trifluoperazine and patient is more or less symptom free.

### DISCUSSION

Patil (1992) first reported the development of transient obsessive-compulsive symptoms in two schizophrenic patients successfully treated with clozapine. Patel & Tandon (1993) also observed the same phenomenon; however, these symptoms were not transient and fluoxetine successfully treated the obsessive compulsive symptoms without compromising the effectiveness of clozapine. Cassidy & Thaker (1993) have also reported usefulness of fluoxetine in such patients. However, Steingard et al. (1993) found that obsessive-compulsive symptoms during clozapine treatment tended to be persistent and response to fluoxetine was variable. Toren et al. (1995) have reported emergence of obsessive-compulsive symptoms in a drug-naive eight year old boy with schizophrenia treated with another atypical antipsychotic-clozapine. However, in treatment refractory OCD, clozapine monotherapy resulted in neither improvement nor worsening of obsessive-compulsive symptoms (Mc Dougle, 1995).

In our cases, obsessive-compulsive symptoms during clozapine treatment of schizophrenics were variable in presentation and course. Case 1 had predominantly compulsive symptoms which were persistent with

clozapine treatment. Case 2 had only obsessive doubts which reduced with clozapine dose escalation. Case 3 had severe obsessive-compulsive symptoms requiring discontinuation of clozapine. We did not use fluoxetine in these cases because some schizophrenic patients with obsessive-compulsive features become more psychotic and disorganised following the addition of serotonin reuptake inhibitor (Lindenmayer et al., 1990). In addition, it has been reported that fluoxetine can lead to marked increase in serum levels of clozapine (Kammen & Marder, 1995) which may indicate that the combination is not safe.

Clozapine is a potent 5-HT antagonist and the data suggest that 5-HT blockade may underlie the development of obsessive-compulsive symptoms in the course of clozapine treatment. "Perhaps, etiologically schizophrenia has several subsets and one of them represents a serotonergic neurotransmitter system in the brain where too little serotonin causes obsessive-compulsive symptoms and too much causes schizophrenic symptoms. It is possible that the mechanism of action of clozapine is its anti-serotonergic property. It is also possible that the 30% of treatment-resistant patients who respond favourably to clozapine represent this subset of schizophrenia" (Patil, 1992).

In the light of still limited knowledge in this field and the multiplicity of central effects of clozapine, we feel that such speculation is premature. Nevertheless, we believe that emergence of obsessive-compulsive symptoms during treatment with clozapine may be more common than reported so far and it is worthwhile to routinely check for such symptoms or else one can misconstrue these as worsening of schizophrenia.

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