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CASE REPORT

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## Olanzapine Treatment after Clozapine Induced Agranulocytosis

Clozapine is an atypical antipsychotic with a significant incidence of agranulocytosis. Olanzapine resembles clozapine structurally; however, it lacks a halogen, which has been implicated in agranulocytosis. Both agents have a similar pharmacological profile. We therefore studied olanzapine in patients with a history of clozapine-induced agranulocytosis. Two patients with severe clozapine-induced agranulocytosis and no benefit from classic neuroleptics were treated with olanzapine with informed consent. Psychosis improved in both patients and no hematological changes were noted. Olanzapine may be a safe treatment alternative in patients with a history of clozapine agranulocytosis. © 1998 John Wiley & Sons, Ltd.

KEY WORDS — olanzapine; clozapine; agranulocytosis

### INTRODUCTION

Clozapine and olanzapine are two atypical antipsychotics. The current indication for clozapine, a dibenzodiazepine, is restricted to therapy-resistant schizophrenic patients because of its risk of developing agranulocytosis which affects approximately 1–2% of all patients within the first year of treatment initiation (Mendelowitz *et al.*, 1995). Olanzapine, a thienobenzodiazepine, resembles clozapine in structural and pharmacological properties (Fulton and Goa, 1997); however, not a single case of agranulocytosis was detected in association with olanzapine in over 3 000 patients enrolled in clinical trials.

We here report two cases of schizophrenic patients who experienced clozapine-induced agranulocytosis and who were switched to olanzapine treatment later on without recurrence of this serious hematological disorder.

TS, a 61 year old male patient, has a long history of schizophrenia, disorganized type. In 1952 he was hospitalized for the first time. He was treated with chlorpromazine and then with a combination of levomepromazine, thioridazine, and clotiapine. In the next decades he was in and out of hospitals and treated with several classical neuroleptics such as haloperidol, trifluoperazine, perphenazine, chlorpromazine, chlorprothixene, and levomepromazine. All treatments failed. In December 1994 all

treatments were stopped and clozapine was administered. Clozapine was titrated up to 200 mg per day within 3 weeks. After a total of 40 days of treatment the neutrophils dropped to 16% and leukocyte count to 1.2 GI/l. Clozapine was stopped immediately, but WBC decreased further to 0.65 GI/l over the next two days. Under treatment with leucomax, mezlocillin and aminoglycoside the patient recovered. From February until November 1995 the patient again received a combination of classical neuroleptics, chlorpromazine, chlorprothixene and clotiapine. In November 1995 treatment with olanzapine was started. Under treatment with olanzapine for 17 months the patient's psychotic condition improved and he did not experience a recurrence of leukopenia or agranulocytosis (Figure 1).

MM is a 66 year old female patient with a long history of treatment-resistant schizoaffective disorder. She had her first psychotic exacerbation in 1956. Until 1988 she was continuously treated with chlorpromazine and lithium. In 1988 lithium was stopped because of signs of congestive heart failure. Numerous treatments were implemented thereafter (haloperidol and ECT, sulpiride and ECT, ECT maintenance, trazodone), but the outcome was poor. In 1992 treatment with clozapine was started. After 48 days of treatment and at a dose level of 100 mg per day she developed agranulocytosis (neutrophils 10.2%) and leukopenia (WBC count

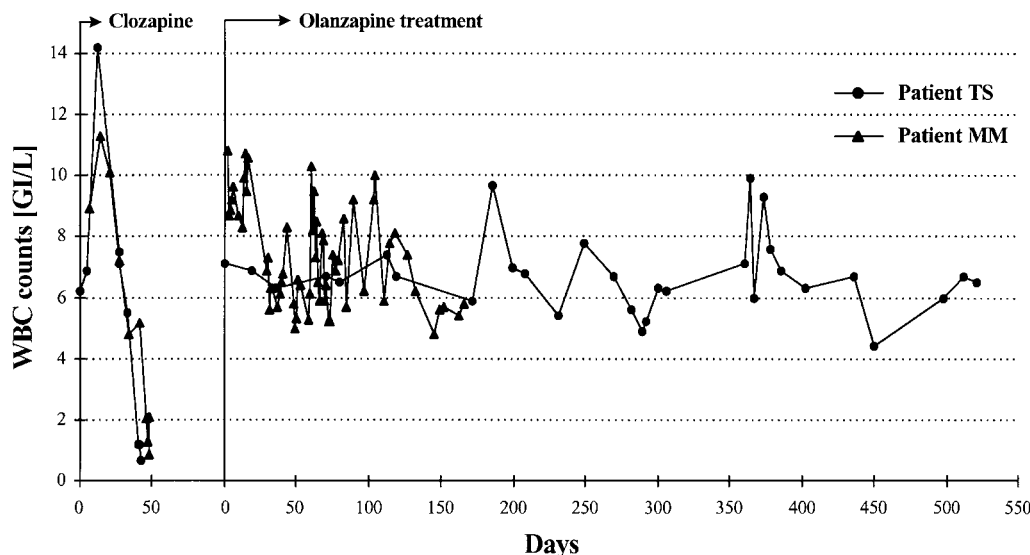


Figure 1. WBC counts under clozapine and olanzapine treatment

0.86 GI/L). She was treated for 27 days in the intensive care unit with interleukin-3, GM-CSF and several antibiotics. After she recovered, various treatments were tried such as levopromazine and ECT, thioxanthenes, perphenazine, clonazepam, fluvoxamine, dibenzepine, and clotiapipe and haloperidol, all with little success. In November 1996 treatment with olanzapine was started. Under treatment with olanzapine her psychotic condition improved and she did not experience any recurrence of agranulocytosis (Figure 1).

## CONCLUSIONS

The case of these two patients (see Figure 1) suggests that there is no cross-reactivity of hematological toxicity between clozapine and olanzapine. Although more clinical experience is needed to confirm this observation, olanzapine may represent a safe treatment alternative for patients who experience clozapine-induced agranulocytosis. Other atypical antipsychotics such as risperidone are also not reported to cause agranulocytosis, but the question arises most acutely with olanzapine

because of its structural and clinical similarity to clozapine.

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