Olanzapine as medication of first choice in therapy-resistant schizophrenia?

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**Summary**

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A case history of a thirty-one year old schizophrenic female who was treated with olanzapine is described. Olanzapine is a relatively new atypical antipsychotic drug with a dopamine antagonistic as well as a potent serotonin antagonistic effect. Olanzapine was prescribed effectively after haloperidol, flupentixol chloride, and clozapine had not led to (lasting) improvements of the psychiatric condition of the patient. Considering the efficacy and the limited risks of this relatively new antipsychotic medication the question arises as to whether olanzapine should be considered as the drug of first choice for patients who do not benefit from treatment with a typical neuroleptic drug.

**Keywords:** Olanzapine, therapy-resistant schizophrenia


Between 5% and 25% of all schizophrenic patients do not benefit from the use of antipsychotic medication.1 Treatment-resistance in schizophrenia, also called refractoriness, has been defined as: "continuing psychotic symptoms with substantial functional disability and / or behavioral deviances that persist in well-diagnosed persons with schizophrenia despite reasonable and customary pharmacological and psychosocial treatment that has been provided continuously for an adequate time period."(p. 552).1 Nowadays, particularly clozapine (Leponex®) is applied in treatment-resistant psychotic patients. However, this drug has a number of adverse side-effects, of which agranulocytosis is the most severe. The risk is minimised by means of regular screening of the hemogram.2 Since the end of 1996 olanzapine (Zyprexa®) is registered in the Netherlands. Olanzapine is an effective 'atypical' antipsychotic drug with a dopamine antagonistic as well as a serotonin antagonistic effect.3,5 The most important characteristic of atypical antipsychotics is the relative absence of acute extrapyramidal side-effects, especially dystonias, as compared to the typical antipsychotics.3,4 Indeed, patients treated with olanzapine suffer from less dystonia, akathisia, and parkinsonic symptoms than patients using haloperidol.4,5 For these reasons, the question arises whether olanzapine should perhaps be considered as the drug of first choice in patients who show no (permanent) effects after treatment with a conventional or 'typical' antipsychotic drug. Below, a case of a thirty-one year old female patient who was consecutively treated with haloperidol (Haldol®), flupentixol chloride (Fluanxol®), clozapine and olanzapine.

CASE HISTORY OF MRS V.

Mrs V., married and mother of a six year old daughter, was hospitalized for the first time in May of 1995: initially because of severe anxiety which prevented her from relaxing. At night she was afraid to go to sleep. At that time Mrs. V. was 29 years old. She felt like she was living in a different world, and was no longer in control of things. She heard voices uninterruptedly, calling her names, cursing and telling her to take her own life or to hurt her daughter. The patient was diagnosed as suffering from a Psychotic Disorder Not Otherwise Specified at that time. After the first admission, two more periods of hospitalization followed in succession within a brief period of time, lasting three and five months. The diagnosis was changed in schizophrenia of the paranoid type. The hospitalizations were interrupted by short episodes.
during which Mrs V. received intensive psychiatric care at home. Initially, Mrs V. was treated with haloperidol. The dosage was built up to 5 mg twice a day. The psychotic symptoms diminished at first, but after a few weeks she experienced a complete relapse. Besides this, Mrs V. complained of side-effects from the haloperidol treatment, especially hypokinetic rigidity in her legs. After the haloperidol medication was gradually reduced and stopped, she was switched to flupentixol chloride, 5 mg once a day. Once more, the symptoms faded initially. On the basis of this development, and in spite of the presence of negative symptoms, the patient expressed the wish to be discharged against advice. In the home environment, however, she soon experienced a relapse, upon which the medication was raised to 5 mg twice a day. Again, after a short remission, a decompensation occurred, leading to re-hospitalization. During this relapse, the patient started suffering from parkinsonistic side-effects for which the patient was prescribed biperiden (Akineton®). In spite of this prescription the patient kept complaining from rigidity. Because of the side-effects, and because the selected classical neuroleptic medications failed to produce permanent positive effects, it was decided to treat the patient with clozapine. After reducing the flupentixol chloride, the clozapine treatment was increased to 400 mg daily. This time, the psychotic as well as the negative symptoms decreased. Unfortunately the improvement was again followed by a relapse after a few weeks. The pattern of initial improvement after the initiation of a new medication, followed by a complete relapse, is a well-known pattern in therapy-resistant schizophrenic patients. At that time her Global Assessment of Functioning (GAF-score) was 40 and it was assumed that the patient needed long term treatment for schizophrenia with the goal to rehabilitate the patient. For this reason, the patient was referred to Psychiatric Hospital Welterhof. During the psychiatric examination a very tense woman was seen. Her awareness was clear and her orientation appeared undisturbed. Mrs. V suffered from imperative acoustic hallucinations and there was a risk of aggressive or self-destructive behavior. Her thinking was slowed, and the content was coloured by hypochondriac and paranoid delusions. Her mood was depressed and the affect was instable. The depressed mood was diagnosed as secondary to the stressful auditory hallucinations. Nevertheless, Mrs V. was prescribed paroxetine (Seroxat®), in addition to her antipsychotic medication. This antidepressant drug did not lead to any (permanent) improvement of her psychiatric condition. By this time the patient, having undergone seventeen months of psychopharmacological treatment, had the appearance of a defective residential patient. She spent most of her time sitting in a chair, smoking cigarettes. She was barely able to take care of herself. After her disappointing experiences with previous medications, it was hard to motivate her once again for yet another medicinal approach. Nevertheless, she declared herself prepared to try olanzapine. The medication was provided in a dosage of 10 mg once a day. On the second day of taking the medication, Mrs V. reported to have the feeling as if she was waking up from a nightmare. Particularly the voices, and the consequential anxiety started to fade away. On the fourth day the patient indicated that, for the first time in eighteen months, she was completely free of auditory hallucinations. She described that she had the feeling that she had definitely reached a turning point in her condition. Earlier improvements had never been experienced in this way. If one looked at the patient, it was almost unimaginable that this was the same woman who only days before looked like a defective schizophrenic residential patient. In view of her past history, there was fear, that another relapse might develop within a few weeks. However, at the time of writing this description (October 15, 1997) the patient has been asymptomatic for ten months, and has resumed her normal life at home. Her GAF-score was stabilized at 80 and her scores on the Positive and Negative Syndrome Scale (PANSS) were: 7 points on the subscale for positive symptoms, 10 points on the subscale for negative symptoms, and 18 points on the subscale for measuring global psychopathology. Besides this, the patient experiences no side-effects from the olanzapine treatment.

CONCLUSION

Possibly that the distinctive profile of olanzapine, with affinity at dopaminergic, serotonergic, muscarinic, adrenergic and histaminergic binding sites, makes the agent especially effective for patients suffering from a broad range of symptoms that are linked to different brain regions. The patient described above was suffering from positive symptoms, negative symptoms as well as comorbid depression. As a result of the presented case, the question raises as to whether a part of the group of schizophrenic residential patients now listed as therapy-resistant, could benefit from treatment with olanzapine.

Literature

8. Akineton®