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Clinical Description
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The Aripiprazole-Clozapine Association in Treatment Ultra Resistant Schizophrenia

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Background

Clozapine remains the reference treatment in resistant schizophrenia. However, its effectiveness is obtained only in 30% to 50% of cases. In the literature, few studies have established therapeutic strategies in these ultra resistant schizophrenic patients [1].

In this clinical case report, we discuss effectiveness of the addition of Aripiprazole to Clozapine as a therapeutic alternative in the treatment of ultra resistant schizophrenia. The effectiveness of this association could be explained by a complementarity of the two molecules in the dopaminergic and serotonergic pathways [2,3].

Clinical Description

We report the case of Mr. A.T, 44 years old, married since one year, having academic grade level, without any somatic illness and no alcohol or psychoactive substance behavior. He suffers from paranoid schizophrenia since the age of 30 years and he was followed since 2005 in psychiatric department of Sousse. He was admitted in 2005 in psychiatric unity during four months for resistant auditory hallucination. The diagnosis of resistant schizophrenia was retained and the patient was treated with 900 mg/day Clozapine without side effects.

Mr. A.T had a good adherence treatment. Compliance has been verified using questionnaire administrated to the patient and a member of his family and using compliance items (items 9, A and B) of the Schedule for the Assessment of Insight -Expanded version (SAI-E).

To evaluate efficacy of treatment, we used the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptom (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS).

Plasma concentrations of Clozapine and the main metabolite Norclozapine were evaluated by High-Performance Liquid Chromatography method (HPLC).

Despite the administration of high doses of Clozapine (900 mg/day) , correct plasma Clozapine concentration and correct plasma Norclozapine concentration (respectively 824 ng/ml and 72 ng/ml), we have achieved only 22% improvement in the BPRS.

Initially, we associate Amisulpride at a dose of 400 mg/day and diazepam at a dose of 15 mg/day to Clozapine without improving productive symptoms after 4 weeks of treatment.

The second alternative was to combine 4 mg/day Risperidone and 15 mg/day Diazepam at the same dose of Clozapine during 20 weeks. No significant clinical improvement was seen. Clozapine and Haloperidol 10 mg/day was also associated but quickly stopped after development of extrapyramidal syndrome.

Finally, when we choose to associate Clozapine 900 mg/day to Aripiprazole at a dose of 10 mg/day, we noted better improvement in positive symptoms with a marked decrease of anxiety and psychotic symptoms. In this association we found improvement of 48% in the SAPS, 42% in SANS and 40% in BPRS.

Conclusion

The results of this clinical case suggest that the addition of Aripiprazole to Clozapine in treatment ultra resistant schizophrenia could be an effective therapeutic alternative. Double-blind studies comparing this association to other alternative therapeutics are needed to confirm this ascertainment.

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