
# The Aripiprazole-Clozapine association in treatment ultra resistant schizophrenia: A case report

M. Gharmoul, J. Nakhli, A. Mtiraoui, S. Ben Nasr
Department of psychiatry, Farhat Hached university hospital, Sousse -Tunisia

***Poster n° EPA 19-0210***

## Introduction and objectives:

Clozapine is the drug indicated in treatment-resistant schizophrenia, but 40–70% of clozapine-treated patients continue to demonstrate partiel clinical response [1].

Various augmentation strategies have been tested, including the use of other atypical antipsychotics, but no clear recommendations can presently be proposed.

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.

## Case presentation:

We report the case of Mr A.T, 44 years old. He suffers from paranoid resistant schizophrenia since the age of 30 years and was treated with 900 mg/day Clozapine without side effects.

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).

## *Results:*

Despite the administration of high doses of Clozapine (900 mg/day), a correct plasma association we found improvement of 48% in the SAPS, 42% in SANS and 40% in BPRSClozapine concentration and correct plasma Norclozapine concentration (respectively 824 ng/ml and 72 ng/ml), we have achieved only 22% improvement in the BPRS.

Finally, when 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 .

## References:

[1] J. A. Lieberman, A. Z. Safferman, S. Pollack et al., “Clinical effects of clozapine in chronic schizophrenia: response to treatment and predictors of outcome,” American Journal of Psychiatry, vol. 151, no. 12, pp. 1744–1752, 1994
[2] Barbui C, Accordini S, Nosè M, Stroup S, Purgato M, Girlanda F, et al. Aripiprazole versus haloperidol in combination with clozapine for treatment-resistant schizophrenia in routine clinical care: A randomized, controlled trial. J Clin Psychopharmacol 2011;31:266-73.
[3] G. Remington, “Augmenting clozapine response in treatment-resistant schizophrenia,” in Therapy-Resistant Schizophrenia, H. Elkis and H. Y. Meltzer, Eds., vol. 26 of Advances in Biological Psychiatry, pp. 129–151, Karger, Basel, Switzerland, 2010.
[4] Chang JS, Ahn YM, Park HJ, Lee KY, Kim SH, Kang UG, Kim YS. Aripiprazole augmentation in clozapine-treated patients with refractory schizophrenia: an 8-week, randomized, double-blind, placebo-controlled trial.Chang. J Clin Psychiatry. 2008 May; 69(5):720-31
[5] K. Karunakaran, T. E. Tungaraza, and G. C. Harborne, “Is clozapine-aripiprazole combination a useful regime in the management of treatment-resistant schizophrenia?” Journal of Psychopharmacology, vol. 21, no. 4, pp. 453–456, 2007
[6] Aleksander CW, Nicolas A, Séverine CW, Ute N, Maria-Eleni S, Philippe C, Chin BE. Addition of Aripiprazole to the Clozapine May Be Useful in Reducing Anxiety in Treatment-Resistant Schizophrenia. Case Reports in Psychiatry Volume 2011, Article ID 846489.

## Discussion:

In the present study, a high dose of clozapine did not result in a reduction of psychotic symptoms despite an effective period, consistent with literature data which report that high doses of clozapine essentially cause much more side effects than clinical improvement [3].

Various augmentation strategies have been tested, including the use of other atypical antipsychotics, but no clear recommendations can presently be proposed [3]. To date, there are no meta-analyses that have globally evaluated the broad array of treatments investigated, which are routinely added to clozapine in the form of augmentation strategies. A limited number of RCTs have been carried out and summarized in more recent reviews.

As an augmenting agent to clozapine, aripiprazole has not been shown to be superior to haloperidol regarding reducing overall symptoms of schizophrenia, but does lead to markedly less neuroleptic side effects [2]. Chang et al., studied augmentation of clozapine with aripiprazole and found significant improvement in the negative symptoms, and significantly lower level of prolactin and triglycerides in the patients treated with the combination [4] .

In the same way, augmentation with aripiprazole has been documented in a retrospective review of case notes of patients with clozapine-resistant schizophrenia.They reported changes with aripiprazole combination in psychotic symptoms, social function and also in weight, total cholesterol, serum glucose, HDL, CGI and GAF score pre-and post-aripiprazole [5]

However, considering the present observations could be due to external factors or to the natural evolution of the illness, a randomized controlled study is required to evaluate the efficacy of the clozapine-aripiprazole combination in cases of treatment-resistant schizophrenia with predominance of anxiety [6].

In this case, a study demonstrated the efficacy of aripiprazole in the treatment of clozapine-resistant schizohrenia with anxiety involvement. An important reduction of anxiety was clinically observed with a marked improvement of psychosocial functioning. This has been explained by the agonist action of aripiprazole on the 5HT1A receptors which could eventually contribute to the antianxiety action that we have observed [3,6].

## 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 are needed to confirm this ascertainment.