Abstract:

Background – Clozapine has become the clear-cut option for treatment resistant patients with schizophrenia after the landmark study by Kane and his colleagues (Kane *et al.*, 1988). However, in the past decade, the evidence on the efficacy of clozapine over other antipsychotic drugs in treating resistant schizophrenia becomes less obvious. Moreover, there is also a subgroup of patients who have shown a suboptimal response to clozapine. Various adjunctive agents have come into clinical practice to augment the effect of clozapine.

Objectives – Studies concerning the general antipsychotic efficacy and effectiveness of clozapine in treating patients with resistant schizophrenia were reviewed in this paper. Studies on clozapine augmentation were also reviewed. With careful examination of these recent studies, there would be more understanding and updated points of view towards the value of using clozapine and its various ways of augmentation in patients with treatment resistant schizophrenia. These help to determine if clozapine remains to be the drug of choice for treatment resistant schizophrenia; and if it fails, the most suitable ways to augment clozapine's effects.

Method – This paper was developed through literature review with access to major electronic databases, using specific keywords, and a number of inclusion and exclusion criteria.

Results – Various studies concerning the use of clozapine and its augmentation have been found. Clozapine is still considered to be the gold standard treatment for patients with treatment resistant schizophrenia given the limited evidence at hand. For clozapine-resistant patients, augmentation with sulpiride, lamotrigine or ethyl-eicosapentanoate (E-EPA) are considered

beneficial.

Conclusion – From this literature review, clozapine (with sulpiride, lamotrigine or ethyl-eicosapentanoate (E-EPA) added in case of augmentation) is the most effective treatment for patients with treatment resistant schizophrenia. This review remains preliminary because of the methodological problems of the original studies and the limitations of this review. Further experimental studies of larger scale are needed to assess and consolidate the effects of clozapine and its various ways of augmentation.