

Efficacy of Longterm Treatment with Clozapine in Refractory Chronic Schizophrenia

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The long-term efficacy of clozapine treatment was examined in an open prospective study, in order to ascertain whether the short-term therapeutic gains of clozapine would persist during long-term maintenance therapy and whether it is safe and well tolerated. We investigated clozapine's efficacy and its side effects in 21 patients with refractory chronic schizophrenia, who had previously been treated with different kinds of classical antipsychotic drugs but with insufficient clinical effect or distressing extrapyramidal side effects, over a one-year period. None of the patients received concomitant medications such as hypnotics or anticholinergics during the study period. Psychopathology and extrapyramidal symptoms were assessed every 4 weeks until the end of the 24 weeks using the PANSS, CGI and Simpson-Angus Scale.

All rating scores demonstrated a significant improvement from the 4th week through the 48th week of the study period compared with the baseline. A clinically significant improvement in both PANSS total and negative scale scores was to start at the 10th month and continue through the 12th month of the study period, compared with the 3rd month period, the standard short-term evaluation period. 16(76.3%) of the 21 patients responded within 9 months with a 20% or more decrease in the total PANSS. Using a 50% or higher decrease in the total PANSS, we found 5 responders, within up to 12 months of treatment. Of these, one responded at 3 months, another one at 9 months, and another three at 12 months. The tolerability of clozapine was generally found to be good. Hypersalivation(81% h, drowsiness (81%) and constipation(57%) were the most common side effects ; all of these side effects showed a significant decrease on 9-12 months of clozapine administration compared with the first three months of drug administration.

These results suggest that clozapine may be a useful antipsychotic drug for the long-term treatment of chronic schizophrenics, despite the need for regular blood monitoring. A trial of clozapine should last 10 months or longer if one wishes to identify the possible responders.