

Letter to the editor

The Italian Clozapine System (ICLOS) for treatment monitoring: more than 2 years of experience

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A database including demographic and clinical information collected from 1,913 patients treated with clozapine in 455 psychiatric services is available in Italy. Demographics are outlined as follows: 62.8% of patients are males and 37.2% females; the mean age is 36.3 ± 11.1 years, the age at onset of illness is 22.3 ± 7.5 , the duration of illness is 14.2 ± 9.5 years and the mean number of hospitalisations before starting the treatment with clozapine is 3.1 ± 6.8 . For 80.1% of patients, a diagnosis of "schizophrenia" according to Diagnostic and Statistical Manual (DSM)-IV criteria has been reported, while no diagnosis is available for the remaining 19.9%. All patients had been withdrawn from previous treatment with typical neuroleptics: 84.2% of them for lack of efficacy (persistence of positive symptoms in 61.7% of patients, of negative symptoms in 50.6% and of poor social adjustment in 55.2%); 40.8% for side effects (34.5% extrapyramidal side effects, 3.3% tardive dyskinesia, 5.9% sedation); 12.7% for lack of compliance, and 4.4% for unspecified reasons.

The mean dose of clozapine used in these patients has been 283.9 ± 133.6 mg/die, with 85.1% of the patients receiving a dose higher than 100 and lower than 500 mg/die. No significant relationship between clozapine doses and side effects has been observed.

Forty percent of patients have been treated with clozapine only; 60% have received adjunctive psychotropic treatment, mainly including benzodiazepines (57.6%) and/or standard neuroleptics (22.3%).

Five hundred and forty-three patients (28.4%) dropped out during clozapine treatment: 110 for lack of efficacy, 116 for non-compliance, 62 for non-haematological side effects, 36 for neutropenia/agranulocytosis, 219 for other reasons

(eg. patient moving to another city or not needing further treatment). The main non-haematological side effects causing treatment discontinuation included fever (16 patients), weight gain (nine patients), increase of liver enzymes (six patients), seizures (three patients), dyspnea (four patients).

Ninety point nine percent of neutropenia/agranulocytosis cases occurred during the first 18 weeks of treatment, 9.1% between the 18th and the 50th week. In 23 patients, neutropenia not associated with any clinical sign or symptom was observed; in 13 cases agranulocytosis was reported, in two patients with hyperthermia. Six patients with agranulocytosis have been treated with either granulocyte or macrophage stimulating factors. In all cases of neutropenia/agranulocytosis, clozapine withdrawal has been followed by complete normalisation of haematological parameters.

In summary, according to the database provided by the Treatment Monitoring System, clozapine in Italy is most frequently used in male chronic schizophrenics. In switching patients from standard neuroleptics to clozapine, clinicians seem to value more the lack of efficacy than the side effects of those drugs. In line with the tendency observed in other European countries [2], low and mean doses of clozapine are preferred to high doses. The possibility that such a tendency contributed to the high rate of drop-outs for lack of efficacy cannot be ruled out and should be addressed by further investigations.

The frequency of agranulocytosis (0.7%) is in line with the data reported in the literature [1]. The favourable outcome of all neutropenia/agranulocytosis cases indicates the usefulness of haematological monitoring carried out weekly during the first 18 weeks, and then monthly.

REFERENCES

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