

Psychopharmacology for the Clinician

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Managing pathologic aggression in people with psychotic disorders

A 55-year-old man had longstanding paranoid beliefs that the police were responsible for his personal bankruptcy. He believed they wanted to kill him through actual or simulated suicide, and he often carried a revolver. After attempting suicide by firearm, delusional disorder and major depression were diagnosed and he started risperidone and citalopram. A few years later, he shot 5 people, killing 1. He believed he saw police officers at his former company and believed they were conspiring to kill him.

An initial forensic assessment led to a diagnosis of schizophrenia, paranoid type, and depressive disorder not otherwise specified. He received a verdict of noncriminal responsibility owing to mental disorder. It was decided that he presented a significant threat to public safety owing to lack of insight into his chronic mental illness and that he would benefit from inpatient therapeutic care and psychotherapeutic feedback. His clinical condition improved with quetiapine and citalopram, but he remained actively paranoid, with increased irritability and defensiveness. He was physically aggressive on 2 occasions, once during a trial with adjunct of aripiprazole. Although he had been reluctant to use clozapine, he eventually consented, hoping that it might improve his quality of life and lead to community privileges. Clozapine was introduced and gradually increased. His condition greatly improved, with decreased paranoia, irritability, hostility and impulsivity. He was eventually allowed to enter the community, indirectly supervised, for specific purposes.

Despite the introduction of new anti-

psychotics in recent years, few studies compare their effectiveness in the management of pathologic aggression.^{1,2} Compared with conventional antipsychotics, clozapine has superior anti-aggressive effects in patients with schizophrenia or schizoaffective disorder,^{1,3-5} including treatment-resistant patients.⁶ A randomized, double-blind study assessing the effects of typical and atypical antipsychotics in the treatment of violent behaviour among inpatients with these disorders demonstrated that clozapine was more efficacious than olanzapine and haloperidol in reducing aggressive behaviour.¹ A subsequent study² reported similar effects on aggressive behaviour, with no effects on cognitive functions.⁷

Treatment with clozapine can be complicated by many adverse effects, such as cardiac complications, nocturnal enuresis, hypersalivation and strong sedation.⁸⁻¹² Seizures, cognitive deterioration/delirium, and obsessive-compulsive symptoms were also noted,¹²⁻¹⁵ and elevated blood cholesterol, weight gain and metabolic complications are common.^{16,17} Potentially life-threatening side effects of clozapine are agranulocytosis, cardiomyopathy, myocarditis, hypersalivation-induced aspiration pneumonia and acute myeloid leukemia.¹⁸⁻²¹ To minimize adverse effects and increase response to clozapine, up-titration should be slow, and patients should be treated with the lowest effective dose.²² Reducing the dose can improve many dose-dependent side effects.

Important principles for the long-term management of violent patients are to ascertain the diagnosis, recognize the risk and not undertreat; the risk of nonintervention may be greater than that of intervention in this population. Persistently aggressive patients show

less improvement in psychopathology,⁶ and their violent behaviour interferes with integration into the community.

The Schizophrenia Patient Outcomes Research Team project provides updated treatment recommendations based on an extensive review of pharmacologic research. The latest update recommends a trial of clozapine in patients with schizophrenia with persistent symptoms of hostility and/or violent behaviour.²³ Yet, we suspect that clozapine may be underused in this population. For example, we are associated with a modern urban mental health centre caring for patients with chronic psychiatric illness. Our schizophrenia and forensic psychiatry programs currently have a similar caseload (1475 v. 1480). In the schizophrenia program, 299 (20%) patients receive clozapine compared with 35 (2%) from the forensic psychiatry program. Although the exact number of patients with a diagnosis of schizophrenia or psychosis has not yet been determined, one suspects that most forensic psychiatric patients, especially those found not criminally responsible, have a major psychotic illness.

Our case illustrates the benefit of clozapine in a psychiatric population at risk for pathologic or severe aggression. This raises the question of whether the use of clozapine should be expanded in the forensic psychiatric population, assuming we are dealing with a large number of psychotic individuals with severe aggression.

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Psychopharmacology for the Clinician columns are usually based on a case report that illustrates a point of interest in clinical psychopharmacology. They are about 650 words long. Columns can include a bibliography which will be available only on the journal website.

A bibliography for this column is available in the online version at cma.ca/jpn.

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