The Association between Schizophrenia and Violent or Homicidal Behaviour: The Prevention and Treatment of Violent Behaviour in These Patients

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ABSTRACT

Background and objective: *This review article aims to discuss and evaluate the risk factors for the development of violence and homicidal behaviour and the effectiveness and outcomes of the preferred atypical antipsychotics in patients diagnosed with schizophrenia.*
Method: *For this purpose, the psychiatry literature was comprehensively reviewed. A screening of the articles in the international databases covering the period between 1970 and 2010 was performed.*
Results: *Although the risk of homicidal behaviours is higher in patients with schizophrenia compared to the overall population, little is known about the relevant conditions triggering acts of violence among the patients with schizophrenia. The available results suggest that certain factors including some socio-demographic characteristics, young age, alcoholism, substance abuse, noncompliance with treatment, fulfillment of the criteria for antisocial personality disorder and paranoid subtype, history of suicidal ideation and attempts and history of frequent hospitalization increase the potential for violent episodes. Available data show clozapine to be the most rational therapeutic choice in preventing violent behaviour in patients with schizophrenia. There is evidence from randomized controlled trials in support of the specific anti-aggressive effect of clozapine.*
Conclusion: *In clinical practice, patients with a risk of committing homicide should be detected and monitored closely. There are many trials showing the efficacy of clozapine on violent and aggressive behaviour.*

Keywords: Atypical antipsychotics, homicide, risk factors, schizophrenia, violence

Asociación entre la Esquizofrenia y la Conducta Homicida o Violenta Prevención y Tratamiento del Comportamiento Violento en Estos Pacientes

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RESUMEN

Antecedentes y Objetivo: *Este artículo de revisión esta dirigido a discutir y evaluar los factores de riesgo en el desarrollo de la violencia y el comportamiento homicida, frente a la efectividad y los resultados de los antipsicóticos atípicos preferidos en pacientes diagnosticados con esquizofrenia.*
Métodos: *Para este propósito, se procedió a hacer una revisión exhaustiva de la literatura psiquiátrica. Asimismo se realizó un análisis y selección de los artículos en los bancos de datos internacionales, abarcando el periodo entre 1970 y 2010.*
Resultados: *Aunque el riesgo de comportamiento homicida es más alto en los pacientes con esquizofrenia si se le compara con la población mundial, poco se sabe de las condiciones pertinentes que desatan actos de violencia entre los pacientes con esquizofrenia. Los resultados disponibles sugieren que ciertos factores – que incluyen algunas características sociodemográficas, edad juvenil, alcoholismo, abuso de substancias, no cumplimiento con el tratamiento, correspondencia con los rasgos de desorden de personalidad antisocial y el subtipo paranoico, historia de ideación e intentos suicidas, así como antecedentes de hospitalizaciones frecuentes – aumentan la potencialidad de los episodios violentos. Los datos disponibles muestran la clozapina como la opción terapéutica más racional para prevenir el comportamiento violento en los pacientes con esquizofrenia. Hay evidencias*

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provenientes de ensayos controlados aleatorios que fundamentan el efecto anti-agresivo específico de la clozapina.

Conclusión: *La práctica clínica debe detectar y monitorear de cerca a los pacientes con riesgo de cometerr homicidio. Hay muchos ensayos que muestran la eficacia de la clozapina en controlar el comportamiento violento y agresivo.*

Palabras claves: Antipsicóticos atípicos, homicidio, factores de riesgo, esquizofrenia, violencia

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INTRODUCTION

The community perception that the mentally ill are dangerous contributes to the stigma experienced by those with schizophrenia, and the risk of homicide by the mentally ill has been used as an argument against deinstitutionalization (1). The relationship between mental illness and violence has been the subject of scientific research for the past 20 years, during which substantial progress has been made in identifying the risk factors empirically related to violence. Some studies appear to support a clear link between mental illness and violence (2).

In the 1980s, expert opinion suggested that there was no increased risk for violence in individuals with schizophrenia and other psychoses (3). However, with the publication of large population-based studies over the last two decades, it is now thought that there is a modest association between violence and schizophrenia and other psychoses (4).

Individuals with severe mental illness commit one in 20 violent crimes (5). Individuals diagnosed with schizophrenia are suggested to be prone to violent behaviours. This suggestion is still controversial (6). Fazel *et al* reported that the Schizophrenia and Related Disorders Alliance of America states that people with schizophrenia were no more likely to be violent than their neighbours, and SANE Australia states that people with mental illness who receive treatment were no more violent than others (7). The issue remains topical because it is thought to have contributed to policy and legal developments for psychiatric patients (8) and the striking increase in the number of secure hospital patients in many Western countries (9). It also contributes to the stigma associated with mental illness (10), which is considered to be the most significant obstacle to the development of mental health services (11). However, the prevalence of persons with schizophrenia committing homicide among all homicide cases was reported to be higher than the prevalence of schizophrenia in the overall population (12−14). Although the prevalence of schizophrenia is usually estimated to be below 1% of the population (15), a three-year monitoring study revealed 85 individuals diagnosed with schizophrenia (5%) among 1594 individuals who had committed homicide (12). These rates raise the question of what are the features in persons with schizophrenia, who have committed homicide, that differentiate them from other persons with schizophrenia. Various trials investigating the sociodemographic and clinical characteristics of the individuals under risk have been conducted. These trials provide elucidative information on individuals who are susceptible to acts of violence against others.

Present data show that clozapine is the best choice of treatment to prevent violence directed behaviour in schizophrenics. Citrome and Volavka concluded in a review that there was encouraging evidence for the anti-aggressive property of clozapine (16). Aleman and Kahn published a meta-analysis in 2001 of seven controlled trials investigating the effect of risperidone on hostility and aggression in schizophrenia. In a sub-analysis, which included five studies, risperidone was demonstrated to be significantly better than typical antipsychotics (17).

This review article aims to discuss and evaluate the risk factors for the development of violence and homicidal behaviour and the effectiveness and outcomes of the preferred atypical antipsychotics in patients diagnosed with schizophrenia.

METHODS

International databases such as PubMed, Ambase and PsychInfo published between 1970 and 2010 were searched using the following terms: schizophrenia, psychosis and violence, homicide, aggression, antipsychotic and neuroleptic. Publications were largely selected from the past 20 years, but commonly referenced and highly regarded older publications were not excluded. We also checked the references of all original papers and reviews obtained. The search was limited to the English language reports.

RESULTS

Evaluation of the risk factors

Patients with schizophrenia comprise between 5% and 20% of all homicide offenders (18, 19). It has been estimated that the average incidence of homicide by the severely mentally ill is about 0.13 per 100 000 per year in most countries (20) although higher rates are found in countries with a higher total homicide rate (21). A recent systematic review found that psychosis increases the risk of violence between two- and seven-fold and the risk of homicide as much as 20 times. Fazel *et al* also found that the risk of homicide in individuals with schizophrenia was 0.3% compared with 0.02% in the general population (7).

The sociodemographic characteristics of mentally ill patients with no criminal responsibility show similarity between the United States of America (USA), Canada and Japan. These cases did not only cover those diagnosed with schizophrenia involved in judicial trials, but all cases of mental disorder without violence. These cases mostly involved the unemployed, poorly educated, single males between 20 and 29 years of age with a history of committed violence, presence of severe psychiatric disorder and a prior judicial and psychiatric history (22).

Fazel and Grann found higher risk estimates in the female-only and mixed gender studies compared with the general population, although these estimates were not significantly higher than in males. The higher risk estimates in women may be a consequence of the lower prevalence of drug and alcohol use in the general female population compared with the general male population, and so violence associated with other causes, including schizophrenia, would be over-represented in the women (23). However, in another trial with a total of 49 patients with schizophrenia who committed homicide, 43 were reported to be males and six were reported to be females. This study revealed a mean patient age of 37 years; the majority of the patients lived in urban areas (61.2%), most of them were poorly educated and 75.5% were unemployed (24).

Some researchers found a series of interrelated factors that suggested that co-morbid depression was related to future homicide. These variables were abnormal mood on ad-mission (25). A German study of violent convictions in patients with schizophrenia after discharge from hospital has also reported inverse associations with depression (26).

One study reported that approximately 25% of the persons with schizophrenia who committed homicide had never presented to a psychiatry clinic previously. Despite this fact, they had been manifesting the clinical signs of schizophrenia for a long time (12). However, the findings in some studies, that a large proportion of the homicides committed by those with psychotic illness occur before initial treatment, suggests that the risk of homicide is higher in the first episode of psychosis than later in the course of illness. Two studies in England and Wales found that 42% and 38% of patients, respectively, with schizophrenia who committed homicides had never been treated, and a study from the Australian state of New South Wales found that 61% of the homicides were committed during the first episode of psychosis (15).

It was suggested that persons with schizophrenia who have shown violent behaviours and committed homicide had high rates of an additional diagnosis of personality disorder (27) and particularly, the antisocial type (28). There is a subgroup of persons with schizophrenia who present a stable pattern of antisocial and/or aggressive behaviour from a young age (29). In persons with schizophrenia, par-ticularly acute positive symptoms were reported to be pre-dominant during the act of homicide (30). In addition, the concomitant presence of persecutory delusions renders the condition more severe in persons with schizophrenia prone to violence. These individuals probably have a history of self-inflicted violence and violent behaviours against others (31). Factors including alcohol abuse (32), substance abuse (13) and non-compliance with medical treatment (33) were found to be associated with violent behaviours and acts of homicide. A trial investigating 49 individuals with schizophrenia who committed homicide showed the following breakdown for those who fulfilled the criteria of paranoid subtype − 42, disorganized subtype − 5, residual subtype – 1 and undifferentiated subtype – 1. A great majority of the cases were patients diagnosed with paranoid schizophrenia. Of these individuals, 42 had reported that they had not been receiving their medication on a regular basis while only 10 had received medication on the day of the homicide (24).

A study analysing 1423 individuals, who had committed homicide in Finland over 12 years, suggested a six-fold higher potential for committing homicide in non-alcoholic persons with schizophrenia compared to normal individuals while the association of alcoholism and schizophrenia could increase this rate up to 17-fold (34). In view of susceptibility to violence overall, early onset of schizophrenia (35), presence of previous suicidal attempts (36), history of frequent hospitalization (37), presence of aggressive behaviours at the time of hospitalization (38) and history of previous judicial aggression are indicators of a severe risk potential (36).

Effects of atypical antipsychotics on aggressive and violent behaviour in schizophrenia

There are many studies showing the efficacy of clozapine on patients with violent and aggressive behaviours. Buckley *et al* (39) demonstrated that clozapine use in two groups of patients with schizophrenia with and without prior history of violent behaviour resulted in a marked reduction in aggressive behaviours during the first six months of treatment in the group with prior history of violent behaviour. A retrospective, open-label trial by Spivak *et al* (40) involving 14 schizophrenic, neuroleptic-refractory patients treated by clozapine for 18 weeks demonstrated a marked reduction in impulsiveness and aggression. Rabinowitz *et al* (41) reported a marked reduction in verbal aggression in 75 patients receiving clozapine in their retrospective, case-based review. Volavka *et al* (42) detected serious effects of clozapine on hostility in their open-label trial including 123 treatment-refractory, schizophrenic patients, where they used the Brief Psychiatric Rating Scale (BPRS). Maier (43) also reported that 52% of the 25 treatment-refractory schizophrenic or schizoaffective patients hospitalized at the forensic hospital improved and reached a favourable status on a forensic basis or showed improvement and were transferred to lower-security units as a result of treatment with clozapine. A prospective trial by Ebrahim *et al* (44) performed in 27

patients, of whom most were paranoid schizophrenic, demonstrated that clozapine treatment provided marked reductions in hostility and aggression.

Two randomized controlled trials (RCT) provide evidence that clozapine has superior efficacy in reducing violent behaviour (45, 46). A third study (47), using data from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project, found no advantage of atypical over typical antipsychotics. However, Phase 1 of the CATIE study did not include clozapine as one of the medications investigated.

Data from the first RCT in support of clozapine were published in 2001 (48) and subsequently in *post hoc* analysis in 2004 (489). It included patients with chronic treatment-resistant schizophrenia and significant ongoing symptoms. Positive and Negative Syndrome Scale (PANSS) was used. Subjects were randomized to clozapine, olanzapine, risperidone or haloperidol for 14 weeks in a double-blind manner. The 22 patients who committed aggressive acts during the pre-randomization period were distributed equally between treatment groups. In the *post hoc* analysis, the Overt Aggression Scale (OAS) was used to record incidents, and a total aggression score, which reflected severity and frequency of incidents, was computed. Clozapine was found to be superior to haloperidol in reducing the likelihood and severity of aggressive incidents, when the first 24 days were excluded from the analysis. There were no other significant differences between medications. Those patients who were aggressive showed less improvement in psychopathology.

In a publication from 2006, Krakowski *et al* provided further evidence in support of clozapine in a population of schizophrenics with a recent history of violence (45). Patients with DSM-IV diagnoses of schizophrenia or schizoaffective disorder (n = 110) were randomized and double-blinded to clozapine, olanzapine or haloperidol for 12 weeks. Inclusion criteria included an episode directed against another person during the current hospitalization, and persistence of aggression. The subjects were closely monitored on a dedicated research ward where the Modified Overt Aggression Scale (MOAS) was used to rate all incidents on three subscales for external aggression. The clozapine group had the lowest total, physical and verbal aggression MOAS scores. Clozapine was superior to haloperidol, but not olanzapine, in reducing aggression against property. Olanzapine was superior to haloperidol in reducing both physical and verbal aggression on MOAS scores.

In addition to the randomized trial evidence, there are a few controlled studies that lend further support to the superior efficacy of clozapine over other atypical antipsychotics. In a retrospective analysis of 331 patients with schizophrenia, Volavka *et al* reported a decrease in overt physical aggression after 47 weeks of treatment with clozapine (50). Other published controlled studies yielded inconsistent results. There are *post hoc* studies reporting the efficacy of atypicals over typical (47), specifically olanzapine and risperidone (51), quetiapine (52) and ziprasidone (53).

DISCUSSION

Individuals with psychotic illnesses are over-represented in homicide offenders, with prevalences reported from 5 (54) to 20% (55, 18). Violent behaviour is frequent in inpatient settings, particularly in those with psychotic disorders (56, 57).

The rates of homicide may be variable on an international basis in the overall population. The rate is 1.8 per 100 000 in England and Wales while it is 5.5 in the USA (58). In a three-year monitoring trial, 85 (5%) of the 1594 individuals with a history of homicide were detected to be diagnosed with schizophrenia (12). These statistical data represent a significant rate. These rates raise the question of which features differentiate persons with schizophrenia, who have committed homicide from other schizophrenic individuals. As for the schizophrenic offenders, little is known about the relevant conditions triggering these acts of violence. However, a number of trials have been conducted on the sociodemographic and clinical characteristics of these patients. These trials provide elucidative data on individuals who are susceptible to violence and may commit suicide; yet, it is still difficult to establish a specific group and determine the risk factors (59). Risk factors may include, presence of the paranoid subtype, low socio-economic level (24), alcohol abuse (32), substance abuse (13), non-compliance with medical treatment (33), active presence of delusions during the homicide (60) and presence of antisocial personality disorder (61).

The relationship with medication adherence may also mediate the association with violent outcomes, particularly if it precedes substance abuse on the causal pathway to violence. The data on medication adherence have reported associations with violence in naturalistic studies (62). Fazel *et al* suggested that schizophrenia and other psychoses were associated with violence and violent offending, particularly homicide and most of the excess risk was associated with substance abuse co-morbidity in their meta-analysis (7). Perhaps the most important research implication is the need for better quality and larger randomized controlled trials for the treatment of substance abuse co-morbidity in schizophrenia (63). A number of implications arise from this review. Especially, the findings highlight the importance of risk assessment and management for patients with substance abuse co-morbidity. In those without substance abuse co-morbidity, the risk of violent crime was modestly elevated with odd ratios ranging from one to five. However, better adjustment for potentially relevant confounders and problems of misclassification (*ie* many of these patients may have undiagnosed and unreported substance abuse) would possibly reduce the observed risk (64). These findings would suggest that violence reduction strategies could consider focussing on the prevention of substance abuse in patients with schizophrenia.

Approximately 86% of the persons with schizophrenia who have homicidal ideation were reported to also have

suicidal ideation (50). A trial showed that 55% of the treatment-refractory aggressive schizophrenics had ideas of self-destructiveness (65). Of course, further comprehensive trials are required to more clearly describe this correlation. In clinical practice, patients with a risk of committing homicide and those with a risk of committing suicide should be separately detected and monitored frequently. This seems to represent a significant community issue.

A survey conducted in England and Wales reported 55%, 22% and 14% of the homicidal acts were respectively against a family member, someone the patient had previously known and someone the patient previously did not know (58). Another trial showed that the majority of the victims (69.4%) were family members and 10 among 40 individuals with schizophrenia committing homicide had killed his/her partner (24). These data showed that family members and friends of risky patients may be under significant danger. However, a study of stranger homicide in England and Wales over a three-year period from 1996 to 1999 found that people with a diagnosis of schizophrenia were responsible for 7.8% of all homicides and 4.3% of the stranger homicides (1). Measures that ensure earlier treatment of psychosis and continued treatment in the community would be likely to prevent homicides of both strangers and family members.

Available data show clozapine to be the most rational therapeutic choice in preventing violence in schizophrenics. There is evidence from randomized controlled trails in support of a specific anti-aggressive effect of clozapine. Adherence to antipsychotic medication is essential to manage violence in schizophrenia, and hence depot formulations may offer a sensible option in high risk patients. As to the choice of antipsychotic, the data support a superior efficacy of clozapine only. It may be effective in preventing the homicidal attempts. The established efficacy of clozapine in these patients may suggest that these patients can be resistant to treatment.

In clinical practice, patients with a risk to violence and committing homicide should be detected and monitored closely. It is plausible that rendering more effective communication might allow earlier intervention and treatment for unrecognized and possibly unrecognizable risk factors for homicidal acts in people with schizophrenia.

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