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Suicide attempts in a prospective cohort of patients with schizophrenia treated with sertindole or risperidone

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Abstract

The incidence of suicide attempts (fatal and non-fatal) was analysed in a prospective cohort of patients with schizophrenia randomly assigned to sertindole (4905 patients) or risperidone (4904 patients) in a parallel-group open-label study with blinded classification of outcomes (the sertindole cohort prospective study – SCoP). The total exposure was 6978 and 7975 patient-years in the sertindole and risperidone groups, respectively. Suicide mortality in the study was low

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(0.21 and 0.28 per 100 patients per year with sertindole and risperidone, respectively). The majority (84%) of suicide attempts occurred within the first year of treatment. Cox's proportional hazards model analysis of the time to the first suicide attempt, reported by treating psychiatrists and blindly reviewed by an independent expert group according to the Columbia Classification Algorithm of Suicide Assessment (both defining suicide attempts by association of suicidal act and intent to die), showed a lower risk of suicide attempt for sertindole-treated patients than for risperidone-treated patients. The effect was statistically significant with both evaluation methods during the first year of randomized treatment (hazard ratios [95% CI]: 0.5 [0.31–0.82], p=0.006; and 0.57 [0.35–0.92], p=0.02, respectively). With classification by an independent safety committee using a broader definition including all incidences of intentional self-harm, also those without clear suicidal intent, the results were not significant. A history of previous suicide attempts was significantly associated with attempted suicides in both treatment groups.

1. Introduction

1.1. Suicide and schizophrenia

Suicide is substantially more frequent in individuals with schizophrenia than in the general population. According to earlier reviews (Miles 1977; Caldwell and Gottesman, 1990), the lifetime risk of completed suicide in schizophrenia reached 10%. Recently, that estimate was reduced to 4.9% by a meta-analysis (Palmer et al., 2005), which covered 61 studies with a total of 48,176 patients, and also confirmed that suicides are concentrated early in the illness course. The risk is particularly high in the first two years of the illness and decreases with time since first hospital admission (Heilä et al., 2005). Suicide attempt rates at the time of first hospitalization are highest in patients between age 16 and 20 and decrease in older patients (Levine et al., 2010). Clinical contact may exert a protective influence, as suggested by the fact that outpatients with schizophrenia commit suicide at a higher rate than inpatients (Helgason, 1990). The first weeks (Qin and Nordentoft, 2005) or months (Rossau and Mortensen, 1997) after hospital discharge are a critical period. Other risk factors include high premorbid socioeconomic class and high IQ (Siris, 2001), better cognitive functioning (Nangle et al., 2006), greater insight into the illness (Schennach-Wolff et al., 2010), living alone, social fragmentation (Evans et al., 2004), and duration of untreated psychosis longer than one year (Altamura et al., 2003).

The association with clinical features is more controversial. Suicide has been associated with severity of hallucinations and delusional thinking, command auditory hallucinations (Heila et al., 1997), thought disorder (Bakst et al., 2010), post-psychotic depression occurring after acute psychotic episodes (Meltzer and Fatemi, 1995) and severity of depressive symptoms (Bakst et al., 2010). Several studies indicate that patients with schizophrenia tend to utilize violent and lethal methods of suicide, in particular jumping from heights. According to one study, fewer patients with schizophrenia plan the suicide, compared to those without the disorder (Kreyenbuhl et al., 2002). Lack of planning would suggest that suicide in schizophrenia is impulsive and occurs when an opportunity becomes available. However, this is debated and a possible bias is that schizophrenic patients tend not to verbalize their intentions. In the general population, completed suicide rates are consistently higher in males than in females (Bray and Gunnell, 2006). This is also the case in patients with schizophrenia (Roy, 1982, Breier and Astrachan, 1984), although the gender difference is significantly less pronounced. Contrary to completed suicides, suicide attempts are observed at the same rate in males and females with schizophrenia (Harkavy-Friedman et al., 2001). A study in three groups of 160 inpatients each, with unipolar depression, schizophrenia, or opioid dependency showed that a positive family history of suicide was associated with a higher risk for suicide attempt, with high-lethality methods, with repeated attempts, and with a number of attempts, while the interaction between family history and diagnostic group was not significant (Trémeau et al., 2005). Finally, one of the most important predictors of suicide in schizophrenia is a history of a recent suicide attempt (Pompili et al., 2007; Bakst et al., 2010; Reutfors et al., 2009).

1.2. The impact of first- and second-generation antipsychotic drugs on suicidal behavior

The literature on the impact of typical or first-generation antipsychotics (FGAs) on suicidal behavior is contradictory (Mamo, 2007; Aguilar and Siris, 2007). This may be due to methodological shortcomings, such as the retrospective design of most studies, lack of treatment randomization, and confounding factors such as comorbidity and polypharmacy (Meltzer, 2001). Earlier studies reported that FGAs might actually increase suicidal ideation (Beisser and Blanchette, 1961), possibly because of antipsychotic induced akathisia and dysphoria. A study in a cohort of 3474 patients with schizophrenia followed over 4 years found that treatment with thioxanthenes was associated with a significant excess of suicide mortality, compared with phenothiazines, butyrophenones, or benzamides (Montout et al., 2002). In contrast, more recent studies have indicated that adherence to any antipsychotic treatment is likely to reduce suicide risk substantially (Haukka et al., 2008). In a register linkage study among first episode patients, the suicide risk of those not currently using any antipsychotic drug was about 37-fold compared to current users (Tiihonen et al., 2006). Further, a prospective case–control study found more self-injurious behavior following discontinuation of depot antipsychotics at 18 months when compared with patients who were maintained on the medication (Johnson et al., 1983). A negative attitude towards treatment (De Hert et al., 2001) and poor