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Depression in schizophrenia: Comparison of first- and second-generation antipsychotic drugs

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Abstract

The aim of this study was to compare the effects of different antipsychotics on depressive symptoms in schizophrenic patients.

The data were drawn from a retrospective, naturalistic, observational study in which 222 subjects diagnosed as being affected by schizophrenia during a re-exacerbation phase received 6 weeks of monotherapy with fluphenazine decanoate, haloperidol decanoate, haloperidol, clozapine, olanzapine, quetiapine, risperidone or l-sulpiride.

The Brief Psychiatric Rating Scale (BPRS), Extrapyramidal Side Effects Rating Scale (EPSE) and Anticholinergic Rating Scale (ACS) were administered at baseline and six weeks after the beginning of the study; depressive symptoms were evaluated using the BPRS items "depressive mood" and "guilt feelings".

All of the antipsychotic drugs led to improvements in the depressive dimension, but this was statistically significant only in the case of fluphenazine decanoate, haloperidol, olanzapine, risperidone and l-sulpiride. A clinical improvement in the depressive dimension significantly correlated with the severity of the psychotic picture and its amelioration. Female patients were significantly more likely to show an improvement in depressive symptoms.

In conclusion, our findings suggest that atypical antipsychotics as a class do not seem to be more effective on the depressive dimension during the course of schizophrenia than typical ones, at least as far as the collected BPRS data are concerned. The only factor that seemed to influence the improvement in depressive symptoms during our study was gender, as females were significantly more likely to improve although there were no between-gender differences in the baseline severity of the clinical picture.

Keywords: Schizophrenia; Depressive symptoms; Antipsychotics; Female gender

1. Introduction

It is generally acknowledged that depressive symptoms represent an important and distinct symptom domain in schizophrenia (Siris et al., 2001), and may occur at any time during the course of the illness (Sands and Harrow, 1999; Siris and Bench, 2003). Most recent research has shown that they indicate a poor prognosis in terms of recovery and reintegration into the community (Resnick et al., 2004), and they clearly play a part in the devastating long-term nature of schizophrenia. Mood state, energy loss, impaired concentration and reduced self-confidence are depressive dimensions that

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materially contribute to the loss of social and vocational capacity experienced by schizophrenic subjects (Siris and Bench, 2003), thus reducing their quality of life (Norholm and Bech, 2006). In other words, people with schizophrenia and concurrent depressive symptoms are significantly more likely than non-depressed schizophrenic patients to use relapse-related mental health services, to be a safety concern, to have greater substance-related problems, and to report poorer life satisfaction, quality of life, mental functioning, family relationships and medical adherence (Conley et al., 2007). The importance and severity of depression in schizophrenia is sustained by the high 10–15% rate of suicide, which is the leading cause of premature death among schizophrenics (Roy, 1990; Hunt et al., 2006).

It has been reported that the prevalence of depressive symptoms during the course of schizophrenia ranges from 25% to 80% (DeLisi, 1990; Mauri et al., 1995; Mauri et al., 1999), depending on the phase of the illness, patient age (Zisook et al., 2006), treatment setting, and the definition of depression (Hausmann and Fleischhacker, 2002).

Some authors suggest that depressive symptoms may be related to schizophrenia when the full-blown psychosis is most evident (so-called "revealed depression") (Hirsh et al., 1990), thus suggesting that the depression may be associated with the psychotic state itself or a subjective reaction to the experience of psychotic decompensation. Furthermore, it has classically been reported that depressive symptoms are induced by neuroleptic therapy in 15–50% of patients ("pharmacogenic depression") (Kapur and Mann, 1992; Bressan et al., 2002), and that "akinetic depression" may be considered a variant of pharmacogenic depression and related to the akinetic syndromes induced by neuroleptics (Van Putten and May, 1978).

Therefore it would be useful to measure neuroleptic side effects, in order to determine if any observed antidepressant action might be a confound of the difference in side effects.

Therapeutic interventions aimed at treating depressive symptoms in schizophrenic patients help to improve individual patients' quality of life and compliance with therapeutic projects. In a number of cases, the choice of an antipsychotic medication may also depend on its "antidepressant" efficacy.

The aim of this study was to compare the effects of different antipsychotics on depressive symptomatology in schizophrenic patients. In particular we compared the effects of three typical antipsychotics (fluphenazine decanoate (FLZ-D), haloperidol decanoate (HL-D) and haloperidol (HL), and five atypical agents (clozapine (CLZ), olanzapine (OLZ), quetiapine (QTP), risperidone (RSP) and l-sulpiride (L-SLP) in a naturalistic setting.

2. Materials and methods

The data were drawn from a retrospective, naturalistic, observational study of 222 subjects (167 males and 55 females) diagnosed as being affected by schizophrenia on the basis of the DSM IV criteria, and admitted to the Psychiatry Clinic of Milan's Ospedale Maggiore Policlinico during a re-exacerbation phase. The patients fell into eight groups, and each received 6 weeks of monotherapy with CLZ ($n=19$), FLZ-D ($n=44$), HL-D ($n=26$), HL ($n=26$), OLZ ($n=54$), QTP ($n=19$), RSP ($n=19$) or L-SLP ($n=15$); the treatment was chosen by the individual clinicians on the basis of the clinical picture. The mean administered doses at baseline (T0) were CLZ 304.89 mg/day (111.65 SD), FLZ-D 22.23 mg/day (6.17 SD), HL-D 11.3 mg/day (5.97 SD), HL 9.68 mg/day (3.93 SD), OLZ 14.95 mg/day (5.60 SD), QTP 489.90 mg/day (186.91 SD), RSP 4.47 mg/day (1.12 SD), L-SLP 279.8 mg/day (44.61 SD). The only other drugs allowed during the study were benzodiazepines in the case of dire necessity.

The protocol was approved by our local Ethics Committee, and the patients or their relatives were asked to consent to having their data accessed for future use at the time they were admitted.

The Brief Psychiatric Rating Scale (BPRS,1988) and Extrapyramidal Side Effects Rating Scale (EPSE,1970) were administered at baseline (T0) and six weeks after the beginning of the treatment (T1). Anti-cholinergic side effects were evaluated on the basis of a check list (ACS) (Altamura et al., 1987). Extrapyramidal side effects were evaluated as: 0–3 = absence of symptom (Simpson and Angus, 1970), 4–10 = mild, 11–18 = moderate and 19–35 = severe. All rating scales were administered by raters who were blinded to the aim of the study; the investigators were trained in the use of the rating scales before the start of the study in order to ensure inter-rater consistency.

Depressive symptoms were evaluated using the BPRS items "depressive mood" and "guilt feelings" of the Depression Factor (Overall and Gorham, 1988; Hausmann and Fleischhacker, 2002; Velligan et al., 2005); each item was scored from 0 to 7 on the basis of the BPRS Rating Scale, and the scores for the two items were averaged in order to obtain a single mean value for each patient. Values of 0–1.9 = no depression; 2–3.9 = mild; 4–5.9 moderate; and 6–7 = severe.

Motor retardation, sedation, was considered a separate item (0–1 = absence of symptom; 2–3 =