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Psychopharmacotherapy and Remission of Patients with Schizophrenia

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A B S T R A C T

Schizophrenia is a clinical syndrome of variable, but profoundly disruptive, psychopathology that involves cognition, emotion, perception and other aspects of behavior. The Remission in Schizophrenia Working Group (RSWG) has defined criteria for symptomatic remission based on achieving and maintaining a consistently low symptom threshold for at least six consecutive months. Aim of our study was to determine which antipsychotic are used in the treatment of patients with schizophrenia, as well as to assess are there differences between patients treated with typical and atypical antipsychotics and how many of them are in remission according to the defined remission criteria. All outtreated patients with schizophrenia treated at the University Department of Psychiatry, University Hospital Osijek in the period of three months were assessed. The patients were divided in two groups, one group of patients treated with typical antipsychotics, and the other group treated with atipycal antipsychotics. All of them were assessed with specially designed questionnaire about sociodemographic data, than with 8 item of PANSS (remission criteria), and with Clinical Global Impression scale. The authors analysed 193 patients with schizophrenia, 65 (33.7%) of them were treated with typical antipsychotics, and 128 (66.3%) patients were treated with atypical antipsychotics. Younger and work active patients are more often treated with atypical antipsychotics. Authors did not found statistically significant differences in two groups of patients regarding the scores on PANSS, CGI and number of patients in remission.

Key words: *schizophrenia, remission, antipsychotics*

Introduction

Schizophrenia is a clinical syndrome of variable, but profoundly disruptive, psychopathology that involves cognition, emotion, perception and other aspects of behavior. The expression of these manifestations varies across patients over time, but the effect of the illness is always severe and is usually long lasting. Clinicans should appreciate that the diagnosis of schizophrenia is based entirely on the psychiatric history and mental status examination. There is no laboratory test for schizophrenia[1].

Schizophrenia is one of the most severe and disabling psychiatric disorders. Antipsychotic drugs offer considerable benefits in controlling symptoms and preventing relapse[2].

The Remission in Schizophrenia Working Group (RSWG) has defined criteria for symptomatic remission based on achieving and maintaining a consistently low symptom threshold for at least six consecutive months[3].

Aim of our study was to determine which antipsychotic are used in the treatment of patients with schizophrenia, as well as to assess are there differences between patients treated with typical and atypical antipsychotics and how many of them are in remission according to the defined remission criteria.

Methodology and Results

All outtreated patients with schizophrenia treated at the University Department of Psychiatry, University Hospital Osijek in the period of three months were assessed. The patients were divided in two groups, one group of patients treated with typical antipsychotics, and the other group treated with atipycal antipsychotics. We considered flufenazine, haloperidole as typical antipsychotics and risperidone, olanzapine, quetiapine and ziprasidone

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as atypical antipsychotics. All of them were assessed with specially designed questionnaire about sociodemographic data, than with 8 item of PANSS (remission criteria), and with Clinical Global Impression scale. Rehabilitation efforts were the same for all patients.

The authors analysed 193 patients with schizophrenia, 65 (33.7%) of them were treated with typical antipsychotics, and 128 (66.3%) patients were treated with atypical antipsychotics. In the group of patients treated with typical antipsychotics 30 of the patients were treated with flufenazine in the doses from 5–15 mg per day, and 35 of the patients were treated with haloperidole in doses from 4–12 mg per day. While in the group of the patients treated with atypical antipsychotics 49 of the patients were treated with risperidone in doses from 4–8 mg per day, 47 of the patients were treated with olanzapine in doses from 10–20 mg per day, 30 of the patients were treated with quetiapine in doses 600–900 mg per day and 2 of the patients were treated with ziprazidone in dose of 80 mg per day.

The authors found statistically significant differences between patients sex as well as in the mean age of the patients treated with typical and atypical antipsychotics. (Table 1) Also in the level of working activity persisted statictically significant difference, as we can see more patients treated with atypical antipsychotics were still working.

Our results also suggest that there is statisticaly significant difference in the duration of psychiatric treatment between those two groups of patients as well as statistically significant difference in the number of visits to the psychiatrist in the last two years. (Table 2.) There was no statistically significant difference between tne number of hospitalisations, and in duration of hospitalization, and in the number of prescribed medications. (Table 2).

Only item from the PANSS remision criteria in which we observed statistically significant difference between two groups of patients was G 9 (Unusal thought content) (Table 3).

TABLE 1
SOCIODEMOGRAPHIC DATA ABOUT TWO GROUPS OF PATIENTS

	Number of patients treated with typical antipsychotics	Number of patients treated with atypical antipsychotics	Statistical significance
Sex	Female 30 Male 35	Female 81 Male 47	U=3326 p<0.05 (NPT-Mann-Whitney)
Age	Mean= 48.54 S=9.79	Mean =44.70 S=11.26	F=5.469 p<0.05 (Anova)
Working Activity	Active 2 Inactive 63	Active 24 Inactive 104	U= 3456 p<0.01 (Mann-Whitney)

TABLE 2
REMARKS ABOUT USED TREATMENTS IN TWO GROUPS OF PATIENTS

Remarks about used treatments	patients treated with typical antipsychotics	patients treated with atypical antipsychotics	Statistical significance
Duration in years	M= 14.83 S= 8.63	M= 9.96 S= 8.39	F= 14.079 p<0.01** (Anova)
Number of hospitalisations	M= 4.31 S= 4.31	M= 4.16 S= 4.09	F= 0.59 p>0.05 (Anova)
Duration of hospitalisations in months	M= 12.57 S= 29.89	M= 5.43 S= 9.05	F= 6.191 p>0.05 (Anova)
Number of visits to psychiatrist in the last two years	M= 7.71 S= 4.74	M= 9.30 S= 5.14	F= 4.374 p<0.01** (Anova)
Number of prescribed psychopharmacs	D=2	D= 2–3	U= 3874 p>0.05 (Mann-Whitney)

TABLE 3
RESULTS ON THE PANSS REMISSION CRITERIA ITEMS

PANSS	Patients on typical antipsycotics	Patients on atypical antipsychotics	Statistical significance
P1 (Delusions)	D=1 (without)	D=1 (without)	U=3878 p>0.05 (Mann-Whitney)
P2 (Conceptual disorganisation)	D=3 (low)	D=3 (low)	U=3881 p>0.05 (Mann-Whitney)
P3 (Hallucinatory behaviour)	D=1 (without)	D=1 (without)	U=4030 p>0.05 (Mann-Whitney)
N1 (Blunted affect)	D=2 (minimal)	D=3 (low)	U=3664 p>0.05 (Mann-Whitney)
N4 (Passive/apathetic social withdrawal)	D=2 (minimal)	D=3 (low)	U=3570 p>0.05 (Mann-Whitney)
N6 (Lack of spontaneity and flow of conversation)	D= 1–2	D=3 (low)	U=3772 p>0.05 (Mann-Whitney)
G5 (Mannerism / posturing)	D=2 (minimal)	D=2 (minimal)	U=3969 p>0.05 (Mann-Whitney)
G9 (Unusal thought content)	D=1 (without)	D=3 (low)	U=3399 p<0.05* (Mann-Whitney)

Authors didn't find statistically significant difference between the group of patients treated with typical and the group of patients treated with atypical antipsychotics in the CGI score, neither in the overall PANSS remission criteria score. (Table 4.)

In our group of patients 98 of them (50.8%) were in remission according to the PANSS

remission criteria. Thirty five (53.8%) of patients treated with typical antipsychotics were in remission and 63 (49.2%) of patients treated with atypical antipsychotics were in remission.

We can conclude that 2/3 of schizophrenic patients were treated with atypical antipsychotics. Younger and work active patients are more often treated with atypical antipsychotics. Authors did not found statistically significant differences in two groups of patients regarding the scores on PANSS, CGI and number of patients in remission.

Discussion

Standard measurment of symptoms and function in schizophrenia patients is crucial for research and practice. Numerous instruments have been developed; however, their use has been limited to the research context[4,5]. Limitations to their use in clinical practice include: time constraints, difficulties for standardized administration, as well as for their analysis and interpretation[4].

A recent review proposed the use of very short versions of well-established instruments for assessing symptomatic remission in clinical pratice, emphasizing both attenuation and disappeearance of symptoms and stability in that clinical situation[3]. This proposal might help overcome most of the difficulties in using standardized symptoms instruments in the evaluation of schizophrenia patients in routine clinical care[4].

Formal assessment of remission in schizophrenia is a crucial outcome both for clinical research and for practice. Such measurement is carried out only in research settings owing to the burden in administration, and difficulties scoring and interpreting the results[4].

The Remission in Schizophrenia Working Group (RSWG) has defined criteria for symptomatic remission based on achieving and maintaining a consistently low symptom threshold for at least six consecutive months[3].

From results of study done by Gasquet et al. remission can be achieved in a high proportion of patients. Factors such as being previously untreated, having paid

TABLE 4
RESULTS ON THE CGI SCALE AND PANSS REMISSION CRITERIA

	Patients on typical antipsycotics	Patients on atypical antipsychotics	Statistical significance
CGI	D=3	D=3	U=3348 p>0.05 (Mann-Whitney)
PANSS remission criteria	D=1	D=2	U=3742 p>0.05 (Mann-Whitney)

employement and taking olanzapine are predictors of remission[6].

We can see in our group of patients 98 of them (50.8%) were in remission according to the PANSS remission criteria. 35 (53.8%) of patients treated with typical antipsychotics were in remission and 63 (49.2%) of patients treated with atypical antipsychotics were in remission.

Acutely ill schizophrenia patients treated with aripiprazole demonstrated a significantly higher rate of symptomatic remission acros 52 weeks compared with haloperidol-treated patients. The similar remission rates among trial completers in both treatment groups, combined with fewer AE-related discontinuations and lower EPS medication use in the aripiprazole group, suggest that better tolerability with aripiprazole may have contributed to superior overall remission rates[7].

Comparing the patients treated with typical and atypical antipsychotics in our study we didn't observe any statistically significant difference in remission rates between patients treated with typical and atypical antipsychotics. We did not observe statistically significant differences in two groups of patients regarding the scores on PANSS, CGI and number of patients in remission.

Recently, the 'Remission in Schizophrenia Working Group' proposed remission criteria consisting of a reduction to mild levels on key symptoms for at least 6 months.

The study done by Emsley et al. applied these remission criteria to a large first-episede psychosis sample in order to 1.determine the rates of remission, 2.explore predictors of remission, and 3. test the external validity of these criteria[8].

The results suggest that the remission criteria, although based solely on core symptom improvement, can effectively identify patients who have a more favorable overall outcome[8]. Several studies presented that emission from the first episode occurs in about 6 months and in about 3 months for later episodes. Hypomania and simple depression predict early remission from the first episode; flat affect and grandiose delusions predict longer episodes and shorter remissions later in the course[9,10].

Further clarification of factors predicting the outcome in schizophrenia is needed.

There is good evidence that poor insight predicts poor outcome, although perhaps not simply as a consequence of poor compliance. Further support is provided for a link between duration of untreated psychosis and long-term outcome. The relationship between cognition and outcome is complex, with specific cognitive deficits apparently predicting particular outcome domains. Early treatment response is closely related to long-term outcome. Outcome studies may be flawed by sample selection bias, and a lack of standardized outcome measures.

Several predictors are potentially modifiable, indicating that they should be targets for therapeutic intervention. More carefully designet studies are needed. Recently proposed criteria for remission are helpful, and should facilitate cross-sample comparisons[8].

According to Mortimer symptom rating scales are now established in schizophrenia research but their scores are not the same as outcome. Symptom rating scale scores can only comprise a limited part of outcome measurement. Standardised remission criteria may present advantages in outcome research[11].

Although schizophrenia refers mainly to an intrinsic biological vulnerability, only maintenence studies with follow-up of 2 years at most are available. Relapses appear unpredictable and occur even after long-term successful remission during antipsychotic treatment.

Since rehabilitation efforts have effects only after long-term endeavours, antipsychotic relapse prevention should be maintained for long periods. It is reasonable to treat patients suffering from schizophrenia and related psychoses for longer periods than indicated by the current guidelines[12].

Conclusion

Until the definition for 'recovery' is further elucidated, factors such as symptom control and remission, and functional aspects of recovery such as improvements in cognition and social functioning, which are quantifiable, should be used as measures of treatment outcome and markers of recovery[13].

Recent work has focused on schizophrenia as a 'deficit' state but little attention has been paid to defining illness plasticity in terms of symptomatic remission.

The introduction of standardized remission criteria may offer significant opportunities for clinical practice, health services research and clinical trials[14,15].

We can conclude that in our sample of patients 2/3 of schizophrenic patients were treated with atypical antipsychotics. Younger and work active patients are more often treated with atypical antipsychotics. Authors did not found statistically significant differences in two groups of patients regarding the scores on PANSS remission criteria, CGI and number of patients in remission.

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PSIHOFARMAKOTERAPIJA I REMISIJA BOLESNIKA SA SHIZOFRENIJOM

S A Ž E T A K

Schizofrenija je bolest koja pogađa sve sfere ličnosti, kogniciju, emocije, percepciju i druge aspekte ponašanja. The Remission in Schizophrenia Working Group (RSWG) je definirala kriterije za simptomatsku remisiju zasnovano na postignutom i zadržanom niskom stupnju simptoma u trajanju barem šest mjeseci. Cilj naše studije je bio odrediti koji su antipsihotici korišteni u liječenju schizofrenije, te da li postoje razlike između bolesnika liječenih tipičnim i atipičnim antipsihoticima kao i utvrditi koliko ih je u remisiji u prema zadanim smjernicama kriterija remisije. Svi ambulantno liječeni shizofreni bolesnici na Psihijatrijskoj klinici, KB Osijek u periodu od tri mjeseca su analizirani. Bolesnici su podijeljeni u dvije skupine, jednu skupinu bolesnika liječenih sa tipičnim antipsihoticima i drugu skupinu bolesnika liječenih sa atipičnim antipsihoticima. Svi su procijenjeni sa upitnikom o sociodemografskim podacima, zatim sa 8 itema PANSS-a (kriteriji za remisiju) i sa CGI ljestvicom. Autori su analizirali 193 bolesnika sa shizofrenijom od kojih je 65 (33,7%) liječeno sa tipičnim antipsihoticima, a 128 (6,3%) sa atipičnim antipsihoticima. Mlađi i radno aktivni bolesnici su liječeni sa atipičnim antipsihoticima. Autori nisu pronašli statistički značajnu razliku između dvije grupe bolesnika na PANSS skoru, na CGI skoru niti u usporedbi bolesnika koji su uremisiji.