SUMMARY

OBJECTIVES: The aim of our study was to assess clinical presentation of early-onset schizophrenia spectrum disoders (EO-SSD), the time to first improvement and efficacy associated with selected atypical (AAPs) and typical (TAPs) antipsychotics, as well as two main side effects – weight gain and treatment-emergent extrapyramidal symptoms (EPSs) during the treatment in patients with EO-SSD.

METHODS: This was a systematic chart review of all patients receiving routine clinical care in our department, with selected AAPs (risperidone, olanzapine, ziprasidone, quetiapine and clozapine) and TAPs (haloperidol, perphenazine and sulpiride), for schizophrenic psychoses, between 1997 and 2007. During this period, our review identified 173 patients (85 males, 88 females; mean age 15.8±1.6 years); their treatment included 297 treatment trials. Data on premorbid adjustment, prodromal symptoms and psychopathology at admission, as well as comorbidity were evaluated based on the patients´ medical records. The time to first improvement could be estimated in 258 treatment trials; of these, 195 (76%) comprised AAPs and 63 (24%) TAPs. The time to first improvement was assessed in agreement with the methodology established for retrospective studies as the number of treatment days prior to the first record of improvement in the patient´s documentation. Treatment efficacy could be evaluated in 125 patients (60 boys, 65 girls; mean age 15.8±1.8 years); of these, 97 (77.6%) patients had been treated with AAPs and 28 (22.4%) with TAPs. Treatment efficacy was evaluated using the CGI (Clinical Global Impression). The CGI-1 (Severity Scale) was assessed at baseline and after 1, 3 and 6 weeks of treatment. The CGI-2 (Improvement Scale) was assessed based on the change in the patients´ clinical status from baseline to Week 3 or 6 depending on the data available. Response was defined as CGI-2≤2 and was evaluated at the end of the treatment trial lasting for at least 3 weeks. Weight changes could be estimated in 109 patients (52 boys, 57 girls; mean age 15.8±1.6 years). The patients were evaluated based on their medical records prior to starting therapy, and after 1, 3 and 6 weeks of treatment. Extrapyramidal side effects could be estimated in 288 treatment trials; of these, 213 (74%) comprised AAPs and 75 (26%) TAPs. Type of EPSs and their treatment as well as discontinuation due to EPSs were evaluated.

RESULTS: Assessment of the clinical presentation revealed that the most frequent psychotic symptoms at admission were delusions (73.6%; mainly non-systematized – 79.7%), followed by hallucinations (53.5%; mainly auditory – 42.1%, intrapsychic – 17.8% and visual – 15.5%) and negative symptoms (44.8%). Poor premorbid adjustment was found in 61.0% and insidious onset of illness in 61.4% of the patients. Non-specific prodromal symptoms were frequent (88.6%). Comorbidity was present in 86 (49.7%) subjects; most frequent were substance abuse – 12.1%, specific learning disorders – 11.0% and attention-deficit/hyperactivity disorder – 11.6%. The mean time to first improvement was 6.9±4.2 days in the AAP group and 5.8±3.5 days in the TAP group; the difference was significant at the trend level (p=0.063). Differences between individual drugs were not significant (p=0.680). Efficacy:

A total of 69% of the patients were evaluated as responders - 68% on AAPs (n=85; risperidone, olanzapine, ziprasidone) and 71% on TAPs (n=14; perphenazine, haloperidol); this difference was significant (p=0.03). The initial mean inclusion CGI-1 score was 5.6±0.6; this score showed a steady decrease in time during the treatment, being significant between all timepoint measures (p<0.001) to the mean CGI-1 3.4±0.9 at Week 6. The difference between AAP and TAP groups in CGI-1 decrease was not significant (p=0.698) and neither were the differences between individual drugs (p=0.220). The mean CGI-2 score was 2.3±0.8; the difference between AAP and TAP groups was not significant (p=0.906) and neither were the differences between individual drugs (p=0.920). Patients presenting with negative symptoms achieved significantly less improvement in CGI-2 scores (p=0.016) and were less likely to respond to the treatment with significance at the trend level (0.065), compared to patients not affected by negative symptoms. Weight changes: During the first week of treatment, the AAP group (n=85; risperidone, olanzapine, ziprasidone and clozapine) gained 1.5% of baseline weight, whereas the TAP group (n=24; haloperidol, perphenazine, and sulpiride) gained only 0.2% (p=0.049). Differences in relative changes between the two groups were not significant at Weeks 3 and 6. Expressed as absolute values, patients on AAPs and TAPs gained an average of 3.4±3.2 kg and 2.0±3.9 kg, respectively, during 6 weeks of their treatment (p=0.335). Only the risperidone, olanzapine, and clozapine groups had sufficient numbers of patients to allow a comparison at the endpoint of the study (Week 6). On average, the patients gained 3.6±2.6 kg on risperidone, 4.4±2.5 kg on olanzapine and 2.1±4.0 kg on clozapine during 6 weeks of treatment (p=0.286). Extrapyramidal side effects occurred during 80 (28%) treatment trials and were present in significantly more patients treated with TAPs (49%) than with AAPs (20%; p<0.0001). With regard to individual drugs, the rates of EPSs were as follows: 71% with haloperidol, 59% with perphenazine, 32% with risperidone, 27% with ziprasidone, 20% with sulpiride and 6% with olanzapine. There were no EPSs in patients treated with clozapine and quetiapine. The treatment discontinuation rate due to EPSs was 6.6%.

CONCLUSIONS: Patients in our sample showed high rates of negative symptoms, poor premorbid adjustment and insidious onset of illness. Analysis of the time to first improvement revealed a significant group level trend indicating that typical antipsychotic drugs have faster onset of action than atypical antipsychotics. There were no differences in efficacy between AAPs and TAPs, as well as between individual drugs, except that significantly more patients treated with TAPs met response status. The weight gain difference between the AAP and TAP groups found in our study was not as large as described in the literature, whereas TAPs were associated with significantly more extrapyramidal side effects than AAPs.

Key words: early-onset schizophrenia, psychopathology, antipsychotics, onset of action, efficacy, weight gain, extrapyramidal side effects.