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P.2.110 The German postmarketing surveillance of risperidone indaily practice: Gender differences with regard to demographic and treatment data

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Methods: In the context of a German postmarketing surveillance on the long term use of risperidone in daily practice, gender differences with regard to demographic and treatment data during the first 3 months of risperidone administration investigated.

Results: 886 schizophrenic patients (452 males and 432 females) were included in the study. More males were single compared to females. Although females were older than males with a longer duration of illness, they showed a higher level of psychosocial functioning. During pevions treatment females showed a higher rate of tardive dyskinesia, whereas male showed disturbed Kognition mor ofter. Druing treatment with risperidone the mean dosage of risperidone administeres was lower in females, however sigificantly only after 1 month (4.9 mg vs 4.6 mg). The percentage of patients discontinuing treatment as well as medication compliance did not differ beween the genders. Minus symptomatology was higher in men throughout the whole treatment period. Symptom improvement in plus and minus symptoms, in psychosocial functioning as well as in extrapyramidal side effects was significantly during the 3-month period, again without gender differences. As well, the therapeutic efficacy of risperidone was rated favorable in both groups.

Conculsion: Risperidone treatment during a 3-month-period was effichacious without differential effects on male and female schizophrenic patients.

P.2.111 D_2 and 5 HT_{2A} receptor binding of different doses of quetiapine in schizophrenics, a pet study

O. Gefvert [1], I.-M. Wieselgren [2], P. Hagström [1], M. Bergström [3], T. Lundberg [1], B. Långström [3], F.A. Wiesel [2], L.H. Lindström [1].
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Quetiapine ('Seroquel'), a dibenzothiazepine is a new anti-psychotic compound under development. In vitro data indicate that it has a similar receptor profile as that of clozapine, except for a much lower affinity for D_4 and muscarinic cholinergic receptors.

Method: We undertook a study in 5 schizophrenic patients. In 4 patients the dose of quetiapine was titrated up to 750 mg/day in one week. The dose was maintained for 21 days. At day 29 two PET scans were then performed two hours after dosing (at steady state) at 09.00 and 17.00. The ligand C^{11}-raclopride was used to estimate D_2 receptor binding in the striatum, and C^{11}-metylspiperone was used as ligand for 5 HT_{2A} receptors in the frontal cortex. After the first two scans the dose of quetiapine was reduced to 450 mg/day and in 3 of these patients a further two PET scans were performed app. 8 days later at the steady state. The fourth patient had the dose of quetiapine further reduced to 300 mg/day before having two more PET scans. In the remaining patient, who was being well-controlled after titration to 450 mg/day, the dose was reduced to 300 mg/day and then to 150 mg/day with two PET scans at the last two levels at steady state...

Results:

Dose of quetiapine (mg)	150	300	450	750
Number of patients (n)	1	2	3	4
D_2 (% striatum)	0	0	31	43
5 HT_{2A} (% frontal cortex)	38	57	74	76

Discussion: A consistent decrease of receptor blockade, on both D_2 and 5 HT_{2A} receptors, could be demonstrated with decreasing doses of quetiapine.

The low values of D_2 blockade at 150 mg and 300 mg are consistent with the clinical findings of these patients deteriorating after dose reduction. They either had to discontinue quetiapine (n = 1) or increase the dose again to achieve symptom control (n = 1). However higher occupancy values can not be ruled out in other patients, at these dose levels, as the low number of patients in this study will not take into the account the possibility of an inter individual variation of D_2 occupancy.

These data confirm the findings of our earlier study that quetiapine binds to both D_2 and 5 HT_{2A} receptors, but with a higher level of occupancy and with a much more withstanding blockade of the serotonin receptors. From these data it is unlikely that quetiapine will cause EPS in the recommended dose range (150–750 mg). Thereby fulfilling one criterion of being an atypical neuroleptic. The lack of EPS has been proposed to be related to a dopamine D_2 occupancy of less then 75% and at the maximum recommended dose (750 mg) is well below this level.

This study has been sponsored by Zeneca Pharmaceuticals, England. 'Seroquel' is a trade mark and the property of Zeneca Ltd.

P.2.114 Aripiprazole, a new typical antipsychotic: Phase 2 clinical trial result

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Aripiprazole is a new atypical antipsychotic now starting world wide Phase III development by Otsuka Pharmaceuticals. Receptor pharmacology showed that aripipazole is a postsynaptic dopamine receptor antagonist as well as presynaptic autoreceptor agonist. The latter action distinguishes aripiprazole from other currently available antipsychotic drugs. Aripirazole also demonstrated affinity for $5HT_2$ receptor. Aripiprazole has a T-max of 3–5 hr with a half life of 50–80 hr. A positron emission tomography (PET) study showed that aripiprazole enters the brain and its binding to the D_2 receptor increases with increasing doses.

Recently completed double-blind Phase II studies were conducted in a total of 410 acutely relapsing hospitalised schizophrenic patients. In study 31-93-202, aripiprazole was titrated up from 5 to 30 mg in 13 days while in study 31-94-202 fixed doses of 2, 10, and 30 mg/day were administered. Both studies were of 4 weeks duration, and haloperidol was used as an active control.

Based on the last observation carried forward (LOCF) analysis, in both studies aripiprazole was superior to placebo in improving the BPRS-total, BPRS-score, CGI-severity, and PANNS-total. Results of the fixed-dose study of 31-94-202 showed that all three aripiprazole doses (2, 10, and 30 mg/day) showed clinical effect in improving the symptoms of acute psychiatric exacerbation of schizophrenia and the 30 mg dose was consinstently more effective than the lower two doses. The 30 mg dose demonstrated a unique early onset of efficacy from week 1 on all efficacy variables including PANSS-negative score.

Aripiprazole was well tolerated. Extrapyramidal symptoms (EPS) as measured by standard scales were comparable to the placebo treatment. In the aripiprazole treatment groups there was no increase in prolactin level or in body weight.

A favorable safety profile combined with data supporting efficacy in the treatment of the positive and negative symptoms of schizophrenia, suggests that aripiprazole may represent an important advance in the management of psychotic disorders.

P.2.115 Depressive symptoms in acute schizophrenia: Evaluation and outcome under new antipsychotics

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Depressive symptoms occur frequently during the course of psychotic disorders. Despite of their high clinical relevance, there is so far no commonly accepted guideline for evaluation and treatment of depressive symptomatology in more acute states of these disorders. However, recent studies with novel antipsychotics seem to yield promising results. Due to the complex nature of psychotic disorders, a substantial overlap of depressive and negative symptoms and the possible confounding with positive symptomatology and treatment-induced extrapyramidal side-effects (EPS) may account for difficulties in discriminating treatment outcome with respect to depressive symptoms.

Based on recent factor-analytical models of schizophrenic symptomatology, the present approach focused on depressive symptoms. Using confirmatory factor analysis (CFA, LISREL 7.20), a baseline model