of chronic schizophrenic patients. 191 hospitalised patients were included in this study. They fulfilled DSM III-R criteria for subchronic or chronic schizophrenia with acute exacerbation. After a 7-day washout period, patients were treated for 6 weeks with 800 mg/d AMI or 20 mg/d H with the possibility to reduce the dose to 600 mg/d or 15 mg/d respectively. Efficacy was assessed with the BPRS, the PANSS Positive and Negative subscales and the Clinical Global Impression (CGI). Neurological safety was assessed using the Simpson Angus scale (SAs), Barnes akathisia scale (BAs) and Abnormal Involuntary Movement Scales (AIMS).

Results: 95 patients were randomised in the AMI group and 96 in the H group. Significantly more patients dropped out of the study in the H group (39) than in the AMI group (25) ($p = 0.04$). ITT analysis showed no statistically significant difference on BPRS total (AMI mean change: 20.9 versus 17.3 for H) and PANSS Positive subscale scores (AMI mean change: 10.4 versus 9.4 for H), although changes were numerically higher in the AMI group. The negative symptoms assessed with PANSS Negative subscale were significantly more improved by AMI (AMI mean change: 7.5 versus 5.1 for H; $p = 0.038$). The response rate (CGI item 2: very much or much improved) in the AMI group was significantly higher than in the H group (62% versus 44%, $p = 0.01$). The efficacy index (CGI item 3), was also significantly superior for AMI compared with H ($p < 0.001$). The severity of extrapyramidal symptoms (SAs) was significantly lower in the AMI group ($+0.06 \pm 0.51$) compared to H group (-0.19 ± 0.70)($p = 0.005$). The global assessment of akathisia (Bas) and symptoms of tardive dyskinesia (AIMS) showed no statistical difference between both groups. Adverse events were more frequently reported in the H group (72 patients with at least one adverse event) than in the AMI group (54 patients), mostly extrapyramidal symptoms. No clinically relevant modifications were observed in biochemistry or haematology tests. Amisulpride showed potent antipsychotic activity in this study, it was significantly superior to haloperidol in improving negative symptoms and induced significantly less extrapyramidal symptoms than haloperidol.

SCHIZOPHRENIA AND IMMUNOINFLAMMATORY PROTEINS

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Objective: The relationships between different immunoinflammatory proteins and clinical status in schizophrenic patients are studied. *Method:* 19 schizophrenic outpatients meeting DSM-IV criteria for paranoid schizophrenia were interviewed in an outpatient clinic. Psychopathology was rated according to PANNS. The same day that psychopathology was recorded a sample of blood was drawn to determine blood levels of the following immunoinflammatory proteins: alpha 1 glicoprotein, ceruloplasmine, alpha 2 macroglobuline and fraction 3 and 4 of the complement. *Results:* A significant positive correlation was found between PANSS' negative subscale and ceruloplasmine and alpha 1 glicoprotein blood levels. The rest of the studied variables (age, sex, number of admissions, age of onset and years of evolution) did not show significant correlations with positive, negative or general psychopathology subscales. *Conclusions:* Ceruloplasmine and alpha 1 glicoprotein blood levels may be useful as biological markers of negative psychopathology in paranoid schizophrenia.

THE EFFECT OF ZIPRASIDONE ON STEADY-STATE PHARMACOKINETICS OF A COMBINED ORAL CONTRACEPTIVE

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Ziprasidone is a novel antipsychotic agent with combined antagonism at $5HT_{2A}$ and D_2 receptors. A double-blind, placebo-controlled, two-way crossover study was conducted to assess ziprasidone's effect on the pharmacokinetics of a combined oral contraceptive. The study was divided into two 21-day treatment periods with a 7-day contraceptive-free interval. A total of 19 healthy female volunteers received 0.15 mg levonorgestrel (LNG) and 0.03 mg ethinyloestradiol (EE) daily on days 1 to 21. On days 8 to 15, the subjects also received either 20 mg ziprasidone or placebo, twice-daily (once-daily on day 15). Plasma samples were collected up to 24 hours post-dose on day 15 for analysis of LNG and EE. Plasma prolactin concentrations were determined pre-dose and 4 hours post-dose on day 15. The pharmacokinetic data showed no statistically significant differences in mean C_{max}, T_{max} and AUC_{24} for EE in plasma when multiple doses of ziprasidone were administered, compared with placebo. There were also no significant differences in mean C_{max} and AUC_{24} for LNG, although there was a statistically significant (but not clinically relevant) difference in mean T_{max}:

Mean pharmacokinetic parameters

	EE			LNG		
	C_{max}* (pg/ml)	T_{max} (hr)	AUC_{24}* (pg·hr/ml)	C_{max}* (ng/ml)	T_{max} (hr)	AUC_{24}* (ng·hr/ml)
Ziprasidone	72	2.9	954	6	2.3	86
Placebo	77	2.3	960	6	1.7	88

*geometric mean

After dosing with ziprasidone, plasma prolactin concentrations pre-dose and 4 hours post-dose were higher than after dosing with placebo. One subject discontinued due to nausea, tiredness, dizziness and vomiting after the first dose of ziprasidone, but no serious adverse events occurred during the study.

CYTOKINES AND SOLUBLE CYTOKINE RECEPTORS IN THE BLOOD AND CSF OF SCHIZOPHRENIC PATIENTS

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Especially the influence of the cytokines to the neurotransmitter metabolism suggests a pivotal role for psychiatric disorders. From that point of view, neuroleptics would be expected to influence immune parameters. It seems that the cellular immune system is less influenced than the cytokine production by neuroleptics. Preliminary results of investigations of the soluble IL-6 receptor (sIL-6R) in schizophrenics show, that the sIL-6R levels are increased in acute unmedicated schizophrenic patients. During neuroleptic treatment sIL-6R levels decrease to the values of controls. Furthermore, results show that the decrease of sIL-6R levels may predict the decrease of schizophrenic negative symptoms during neuroleptic treatment [1]. In contrary, sIL-2R show an increase in schizophrenic patients during neuroleptic therapy. This result fits with the suggested IL-2-antagonistic function of sIL-2R; IL-2 is described to be elevated in the CSF of schizophrenics and to predict a schizophrenic relapse [2,3]. Moreover, in-vitro studies of the neuroleptic action to cytokines, which underline these

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