approach, 59% of AMI patients and 55% of HAL patients maintained efficacy up to 12 months (Kaplan-Meier estimates, log rank 0.58). When time course of mean BPRS total scores of all patients (LOCF) was compared, AMI was superior to HAL from the third month of treatment. On an intent to treat basis, AMI was superior to HAL in total BPRS score (mean change from baseline 17.0 ± 15.8 vs 12.8 ± 15.5, $p < 0.01$), PANSS Negative subscore (mean change from baseline 7.1 ± 7.7 vs 3.7 ± 7.4, $p < 0.01$) and quality of life (all dimensions of the QLS). AMI provoked significantly less EPS than HAL and correspondingly less antiparkinson drugs were prescribed to AMI patients. Overall, AMI was safe and efficacious in the long-term treatment of schizophrenia.

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AMISULPRIDE IMPROVES AFFECTIVE SYMPTOMS IN ACUTE SCHIZOPHRENIA

W. Rein[1], O. Fleurot[1], S. Turjanski[1]*. [1]*Synthélabo, Bagneux and Le Plessis, France*

Affective symptoms are frequently associated with symptoms of psychosis in schizophrenic patients and represent together with negative symptoms a considerable burden for rehabilitation. Furthermore, suicide is a frequent complication of schizophrenia. Affective symptoms, measured with the BPRS anxiety/depression subscore (items: depressive mood, guilt feelings, anxiety, somatic concern), were assessed during four short-term studies in acutely ill schizophrenic patients (DSM III-R/IV). Amisulpride (AMI 400–1200 mg/d) was compared with haloperidol (HAL 15–20 mg/d, 2 studies), flupenthixol (FLU 15–25 mg/d) and risperidone (RIS 8 mg/d). A total of 870 patients were included, 535 treated with AMI, 160 with HAL, 62 with FLU and 113 with RIS. The mean duration of illness was about 10 years. The baseline scores of the BPRS anxiety/depression subscale varied between 11.1 ± 3.9 and 13.2 ± 4.5. Mean improvement of this subscore was 5.0 (CI 95%: 3.8; 6.1) and 4.5 (CI 95%: 3.5; 5.5) with AMI 400–800 mg/d versus 3.3 (CI 95%: 2.2; 4.4) and 3.1 (CI 95%: 2.0; 4.1) in the HAL groups (for both studies $p < 0.05$). In the study vs FLU, the improvement was 5.6 (CI 95%: 4.6; 6.6) for AMI and 3.6 (CI 95%: 2.6; 4.7) for FLU ($p < 0.05$). The improvement with AMI was also greater in the study vs RIS but this difference did not reach statistical significance: mean change AMI 3.2 (CI 95%: 2.5; 3.9) vs RIS 2.7 (CI 95%: 2.0; 3.5).

The results show that amisulpride improves affective symptoms more than the standard neuroleptics haloperidol and flupenthixol in acutely ill schizophrenic patients.

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AMISULPRIDE IN SCHIZOPHRENIA: A REVIEW OF ITS EFFICACY IN ACUTE AND CHRONIC PATIENTS

H.J. Möller[1], W. Rein[2], S. Turjanski[2]*. [1]*Department of Psychiatry, University of Munich, Germany*
[2]*Synthélabo Groupe, Le Plessis, France*

Amisulpride (AMI) is a D2/D3 specific antipsychotic with limbic selectivity. Its efficacy has been demonstrated in both ptients with acute exacerbations of schizophrenia and in chronic schizophrenia with predominant primary negative symptoms. A total of 870 patients, 535 treated with AMI (100–1200 mg/d) have been included in four short-term studies to assess efficacy in acute schizophrenia (DSM III-R/IV) compared with haloperidol (HAL 15–20 mg, 160 pat.), flupenthixol (FLU 15–25 mg, 62 pat.) and risperidone (RIS 8 mg, 113 pat.). BPRS total score was the primary efficacy endpoint. Negative, affective and extrapyramidal symptoms were also measured. Pooling of data in this studies showed that AMI was at least as efficacious as the comparator drugs: mean change of BPRS total score in the pooled AMI patients was 21.7 (CI 95%: 20.2; 23.3) versus all comparators 16.7 (CI 95%: 14.9; 18.4). The difference between AMI and the comparators was significant 5.1 (CI 95%: 2.7; 7.4, $p < 0.05$). Another series of four studies was performed in chronic schizophrenic patients (DSM III-R) with predominant negative symptoms and absent or low grade of positive symptoms. This type of patient is particularly difficult to treat and a major challenge in the management of schizophrenia. A total of 514 pat. were included, 312 treated with AMI (50–300 mg/d) and 202 with placebo. In all studies AMI was significantly superior to placebo in the main efficacy variable, the SANS total score. The size of improvement reached from 31% to 42% of baseline in the AMI groups vs 8% to 23% in the placebo groups. Positive symptoms, parkinsonism and depression were of low intensity at baseline and did not change notably over time, so that an influence of these factors on the improvement of negative symptoms is improbable.

Overall, AMI provides a wide spectrum of therapeutic activity from acutely ill to chronic patients with predominant negative symptoms.

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AMISULPRIDE — LONG-TERM SAFETY

M. Colonna[1], S. Turjanski[2]*, L. Dondey-Nouvel[2]. [1]*Department of Psychiatry, University of Rouen;* [2]*Synthelabo, Le Plessis-Robinson, France*

In a multicentre, international, open randomised, long-term study, amisulpride (AMI) was compared with haloperidol (HALO). Patients with acute exacerbation of schizophrenia (DSM III-R) were treated for 12 months. A total of 488 patients were exposed to the study drug: 370 to AMI and 118 to HALO. Flexible doses of 200 to 800 mg/d (up to 1200 mg/d) were used for AMI and 5 to 20 mg/d (up to 30 mg/d) for HALO. At the end of the study, mean daily doses were: 605 ± 267 for AMI and 14.6 ± 7 mg for HALO.

Completers were 55% in AMI group and 48% in HALO group. The drop-out rate for safety reasons was higher with HALO (10.2% vs 8.1%). Incidences of open reporting of side effects were similar for both compounds. Extrapyramidal side effects were reported at a higher frequency in HALO group (40.7% vs 25.9%). Endocrine events were low for both drugs (4.1% AMI and 2.5% HALO), and weight increase was higher in AMI group (increase of >5% from basal weight: AMI 32% and HALO 18%).

Simpson Angus scale showed statistically significant differences in favour of AMI, either at the endpoint and at the maximal score ($p = 0.0001$). The difference was also observed with Barnes Akathisia scale at the endpoint ($p < 0.001$). Tardive dyskinesia (AIMS) was less induced by AMI ($p = 0.014$).

Prolactin levels were increased with both drugs, but higher levels were obtained with AMI. Neither AMI, nor HALO increased above 500 ms the QTc, and only 2 patients in AMI group had a QTc increase of at least 60 ms compared with baseline. Laboratory parameters did not show relevant differences between two drugs.

In conclusion, amisulpride showed similar incidence of adverse events compared with haloperidol but a better neurological side-effect profile. Safety in long-term exposure did not differ from that observed in short-term trials.

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