P02.20

Smooth and safe transition from intramuscular to oral olanzapine

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Objective: The efficacy and safety of transitioning patients from IM to oral olanzapine and haloperidol were compared.

Method: Acutely agitated schizophrenic inpatients were treated with 1–3 IM injections/24 hours of olanzapine (10.0mg/injection) or haloperidol (7.5mg/injection) followed by the oral formulations of the same medication (5–20mg/day) for 4 days.

Results: IM olanzapine reduced agitation (PANSS-excited component [PANSS-EC]), significantly more than IM haloperidol 15, 30, and 45 minutes after the first injection. Mean PANSS-EC changes for olanzapine- (n=122) and haloperidol-treated (n=116) patients, respectively, were -7.1 and -6.7 at the 24-hour IM endpoint, with further changes of -0.6 and -1.3 during oral therapy (not significantly different). Significantly more haloperidol- than olanzapine-treated patients spontaneously reported acute dystonia (4.3% vs. 0%, p=0.03), extrapyramidal syndrome (6.9% vs. 0.8%, p=0.02), and akathisia (5.2% vs. 0%, p=0.01) and met criteria for treatment-emergent akathisia (18.5% vs. 6.5%, p=0.02).

Conclusion: Olanzapine reduced agitation more rapidly than and as effective as haloperidol during the IM period. This reduced agitation was maintained by both agents during the transition from IM to oral therapy; however, haloperidol-treated patients experienced significantly more EPS-related adverse events.

P02.21

Risperidone and quetiapine for treatment-resistant schizophrenia

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The aim of our open label study was to investigate the efficacy and the tolerability of risperidone and quetiapine in the treatment of a group of patients with resistant schizophrenia to conventional antipsycotics. 35 patients (21 males and 14 females), aged between 21 and 51 years, were selected for risperidone or quetiapine treatment according to the following criteria: a) DSM IV diagnosis of schizophrenia; b) duration of illness more than 3 years; c) poor response to typical antipsycotics (i.e. persistence of positive and/or negative symptoms, intolerable side effects , especially extrapyramidal symptoms).

Of these thirty-five selected patients, 20 were treated with risperidone (dose 4 – 6 mg/d.), while 15 with quetiapine (dose 150 – 750 mg/d.) for 8 weeks.

Assessments were made at baseline, 4 and 8 weeks, including PANSS, CGI, ESRS and clinical laboratory tests.

The 8-week trial was completed by all the patients. At treatment endpoint both risperidone and quetiapine produced a statistically significant improvement from baseline in the total PANSS score, in all three subscale scores, as well as in CGI score. No significant differences between groups were evident in all efficacy scales, however the quetiapine patients had a better outcome for extrapyramidal side effects, assessed by means of the ESRS.

In conclusion our data indicate the equal effectiveness of quetiapine and risperidone with a better tolerability for quetiapine.

P02.22

Neurocognitive effects: aripiprazole vs olanzapine in stable psychosis

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This multicenter, open-label study compared neurocognitive effects and safety of aripiprazole, the first next-generation atypical antipsychotic, a novel dopamine-serotonin system stabilizer, with olanzapine. Outpatients with clinically stable schizophrenia or schizoaffective disorder were randomized to once-daily aripiprazole 30 mg (n=128) or olanzapine 15 mg (n=127). Neurocognitive assessments were conducted at baseline, weeks 8, and 26. Results were reduced into three factors: general cognition, secondary verbal memory, and executive functioning. The general cognitive factor improved significantly with both medications at week 8. Aripiprazole produced significant within-group improvements in secondary verbal memory at weeks 8 and 26 ($p<0.001$); olanzapine did not. There were no significant changes in executive functioning. There was one significant between-group effect for cognition: aripiprazole was superior to olanzapine on secondary verbal memory at both time points ($p<0.04$). Clinically significant weight gain (>7% increase from baseline) occurred more frequently with olanzapine (27%) than aripiprazole (7%). Aripiprazole demonstrated a significant reduction in mean cholesterol levels compared with olanzapine. The neurocognitive benefits of aripiprazole bode well for psychosocial rehabilitation and may result in health advantages, greater treatment adherence, and reduced relapse rates.

P02.23

Calming versus sedative effects of IM olanzapine in agitated patients

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Objective: Calming versus sedation among intramuscular olanzapine-treated patients were compared with IM haloperidol-, lorazepam-, and placebo-treated patients.

Method: In three double-blind studies, acutely agitated patients with schizophrenia (N=311), bipolar mania (N=201), or dementia (N=206) were treated with 1–3 IM injections of olanzapine 2.5 to 10.0 mg/injection, haloperidol 7.5 mg/injection, lorazepam 2.0 mg/injection, or placebo over 24 hours. Sedation was assessed using the Agitation-Calmness Evaluation Scale (ACES©) and treatment-emergent adverse events.

Results: Across all studies, only one patient (lorazepam-treated, bipolar) achieved an ACES score of unarousable. There were no significant between-group differences in ACES scores of deep sleep or unarousable at any time across each study. When patients who were asleep were excluded from the agitation analyses, PANSS-EC scores remained significantly reduced with olanzapine compared to placebo. The incidence of adverse events indicative of sedation was not significantly different with olanzapine versus active comparator or placebo.

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Conclusions: IM olanzapine-treated patients experienced no more sedation than haloperidol- or lorazepam-treated patients in the treatment of acute agitation associated with schizophrenia, bipolar mania, or dementia, and experienced distinct calming rather than non-specific sedative effects.

P02.24

QTc intervals: IM olanzapine treatment in acutely agitated patients

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Objective: QTc interval data during IM treatment were analyzed among patients with schizophrenia, bipolar mania, and dementia.

Method: In four double-blind trials, patients received 1–3 IM injections of olanzapine (2.5–10 mg/injection), haloperidol (7.5 mg/injection), or placebo over 24 hours. Databases included: placebo-controlled (2-schizophrenia, 1-bipolar), haloperidol-controlled (2-schizophrenia), and geriatric placebo-controlled (1-dementia). Mean QTc interval changes from baseline and prolonged QTc intervals (endpoint >=99% of healthy adults or increase >=60 msec or endpoint >=500 msec) were analyzed.

Results: Overall, QTc interval changes in IM olanzapine-treated patients were small and not significantly greater than placebo. There were significant ($p<0.05$) between-group mean change differences in the haloperidol-controlled database at 2 hours and geriatric placebo-controlled database at 2 and 24 hours after the first injection. The incidences of prolonged QTc intervals for olanzapine-treated patients were never significantly greater than placebo and were <=3% in all databases (exception: <=11% geriatric).

Conclusions: Changes in QTc intervals in IM olanzapine-treated patients were no worse than with placebo, suggesting that IM olanzapine has a favorable QTc interval profile in acutely agitated patients with schizophrenia, bipolar mania, or dementia.

P02.25

Risperidone and olanzapine in inpatient treatment of bipolar disorder

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Objective: To compare drug usage, costs and outcomes in inpatient treatment of bipolar disorder with risperidone (RIS) or olanzapine (OLA).

Method: A retrospective multicenter cohort study using patient chart review. Inclusion criteria were: diagnosis of bipolar disorder, discharged or at least 120 days of follow-up, $\geqslant$ 65 years of age and treated with either RIS or OLA.

Results: 62 patients (RIS=30, OLA=32) were included. Demographic characteristics for the two samples were similar. The median time to onset of efficacy was 9 days for RIS and 12 days for OLA. The average daily dose for RIS was 3.0 mg and with OLA 11.0 mg. 10% of RIS-treated and 16% of OLA-treated patients discontinued therapy.

Daily costs of the studied medication were 4.6 USD for OLA and 2.0 USD for RIS ($p<0.0001$). Daily costs for all in-patient drug use were 6.2 USD in the OLA group and 2.9 USD in the RIS group ($p<0.0001$).

Conclusions: RIS and OLA were both effective in the bipolar patients studied. Drug costs for patients receiving RIS were significantly lower than costs for patients receiving OLA.

P02.26

Atypical antipsychotics in schizophrenia and mood disorder

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Objective: To compare the outcomes associated with atypical antipsychotic treatment in inpatients with schizophrenia and mood disorder.

Method: A retrospective cohort study using patient chart review was undertaken in inpatients diagnosed with schizophrenia or mood disorder, under 66 years of age and treated with either risperidone (RIS) or olanzapine (OLA).

Results: 2013 patients with schizophrenia (N=1901) and mood disorders (N=112) were included. Schizophrenia patients typically had an earlier age of onset of symptoms (24.5 years) than those with mood disorder (30.1 years, $p=0.0002$), and were commonly taking more antipsychotics on admission. Mood disorder patients received lower doses of RIS or OLA ($p<0.0001$), had a shorter time to achieve efficacy ($p=0.01$), were more often discharged within 120 days ($p=0.02$) and had a shorter median time-to discharge ($p<0.0001$) than patients with schizophrenia. Adjusting for background factors had little impact on the dose comparison, time-to discharge or time-to efficacy analyses.

Conclusions: Patients with mood disorders generally required lower doses of atypical antipsychotic and were discharged faster than schizophrenic patients. Differences in clinical outcomes were not explained by differences in background characteristics.

P02.27

Meta-analysis of the efficacy of aripiprazole in schizophrenia

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Aripiprazole is the first of the next generation of atypical antipsychotics. This meta-analysis presents efficacy data from four 4- to 6-week multicenter, double-blind, controlled studies involving 1540 patients hospitalized with acute relapse of schizophrenia or schizoaffective disorder. Patients were randomized to aripiprazole (n=893), placebo (n=380), or active control (haloperidol 10 mg/day [n=167] or risperidone 6 mg/day [n=100]). Daily aripiprazole doses were 2 mg (n=59); 10 mg (n=165); 15 mg (n=207); 20 mg (n=199); 30 mg (n=263). Weekly efficacy assessments included PANSS and CGI. Aripiprazole demonstrated statistically superior antipsychotic efficacy to placebo, as did haloperidol and risperidone. In the meta-analysis, aripiprazole doses over 2 mg produced significant improvement in PANSS-total score by week 1 ($p<0.05$). In individual studies, aripiprazole 15, 20 and 30 mg consistently produced significant improvements in PANSS-total score, with similar changes from baseline observed for all treatment groups. Aripiprazole 15, 20 and 30 mg consistently produced significant improvements in other efficacy scores compared with placebo. These data suggest that aripiprazole improved positive and negative symptoms of schizophrenia disorder, with significant effects present one week after starting treatment.

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