NEW RESEARCH

NEW RESEARCH ABSTRACTS

AMERICAN PSYCHIATRIC ASSOCIATION

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ABSTRACTS

Methods: A total of 249 inpatients with schizophrenia were randomly assigned to receive olanzapine plus placebo, olanzapine plus divalproex, risperidone plus placebo, or risperidone plus divalproex in a double-blind 28-day multi-center trial. Target daily dose was 15 mg for olanzapine, 6 mg for risperidone, and up to 30 mg/kg (minimum 15 mg/kg) for divalproex. The Positive and Negative Syndrome Scale (PANSS) was the principal efficacy measure.

Results: The PANSS Total and the PANSS Positive subscale scores of patients receiving combination therapy with divalproex indicated significantly greater improvement than those of patients receiving antipsychotic monotherapy. This was evident as early as Day 3 (ANOVA, $p<0.05$) and was present throughout the 28 days as demonstrated using repeated measures ANOVA (PANSS Total Score $p=0.020$; PANSS Positive Subscale $p=0.0020$). Adverse events and rates of discontinuation were similar between the treatments.

Conclusion: Divalproex significantly enhances antipsychotic efficacy in patients with schizophrenia. Combination therapy with divalproex was as well tolerated as monotherapy with olanzapine or risperidone.

NR317 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Pharmacokinetics and Safety of Aripiprazole and Concomitant Mood Stabilizers

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Summary:

Objective: To assess the safety profile and pharmacokinetics of aripiprazole, an antipsychotic with a unique pharmacologic profile of dopamine D_2 partial agonism, serotonin $5HT_{1A}$ partial agonism and $5HT_{2A}$ antagonism, when coadministered with lithium or divalproex sodium.

Methods: Two open-label, sequential treatment design studies were conducted in chronically institutionalized patients with schizophrenia or schizoaffective disorder requiring treatment with lithium (n=7) or divalproex sodium (n=6). Patients received aripiprazole 30 mg/day on Days 1–14 and aripiprazole with concomitant therapy on Days 15–36. Lithium was titrated from 900 mg until serum concentrations reached 1.0–1.4 mEq/L for ≥5 days. Divalproex sodium was titrated to 50–125 mg/L.

Results: Coadministration with lithium increased mean C_{max} and AUC values of aripiprazole by about 19% and 15%, respectively, while the apparent oral clearance decreased by 15%. There was no effect on the steady state pharmacokinetics of the active metabolite of aripiprazole. Coadministration with divalproex sodium decreased the AUC, C_{max} and C_{min} of aripiprazole by 24%, 26%, and 22%, respectively, with minimal effects on the active metabolite.

Conclusion: Aripiprazole can be administered safely with therapeutic doses of lithium or divalproex sodium in patients with schizophrenia or schizoaffective disorder.

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The InterSept Scale for Suicidal Thinking: Reliability and Validity

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Summary:

Background: The InterSePT Scale for Suicidal Thinking (ISST) is a 12-item instrument for the assessment of current suicidal ideation in patients with schizophrenia or schizoaffective disorder. We report the psychometric characteristics of this new scale based on two studies.

Method: In Study 1, 22 inpatients with schizophrenia or schizoaffective disorder who had recently attempted suicide or engaged in suicidal ideation were rated by 3 trained independent raters to calculate interrater reliability. In Study 2, 980 patients with schizophrenia or schizoaffective disorder with a history of suicidal ideation in the past 36 months were enrolled in a 2-year industry-sponsored suicide prevention study. At baseline, these patients were administered the ISST by the Principal Investigator (PI) and by a blind rater (BR), the Positive and Negative Symptom Scale (PANSS), the Calgary Depression Scale (CDS), and the Clinical Global Impression Scale for Severity of Suicidality (CGI-SS). Indices of internal reliability, construct and discriminant validity were examined.

Results: The interrater agreement (ICC) for the total ISST score for in Study 1 was 0.90 and mean weighted item kappa coefficients ranged from 0.66–0.92. In Study 2 internal reliability (Cronbach alpha) for all items was 0.88. The ISST (PI) total score was highly correlated with the CGI-Severity of Suicidality by the blind rater ($r=0.86$, $p<0.0001$). ISST total scores significantly differentiated the different levels of CGI-SS ($F=519.3$; $df=4,955$; $p<0.0001$). Results of construct and discriminant validity analyses are also presented.

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Do Atypicals Change the Syndromal Profile in Treatment-Resistant Schizophrenia?

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Summary:

There has been considerable support for the observation that atypicals have a different pattern of clinical effects than traditional antipsychotics. We are exploring whether this difference can also be seen in treatment-resistant schizophrenia. We are presenting data from two PANSS-based factor analyses (baseline and endpoint) from a prospective, double-blind, randomized 14-week trial in which 157 inpatients with DSM-IV treatment-resistant schizophrenia or schizoaffective disorder were assigned to either clozapine, olanzapine, risperidone, or haloperidol. We found both at baseline and endpoint a five-factor solution based on principal component analysis of the 30 PANSS items and after orthogonal factor rotation. While treatment was associated with an overall modest change, there was a change in the amount of variance explained by the excitement, cognitive, positive and depression/anxiety factors explaining 60% of the variance. At endpoint, the largest variance was explained by the cognitive factor followed by the excitement, positive, negative and depression/anxiety factors explaining 59% of the total variance. This change meant that negative symptoms contributed less to total psychopathology, while cognitive symptoms were more predominant after treatment with atypicals. The implications of these findings in comparison with results from studies with treatment responsive patients are discussed.