P-10-22

Neurocognitive differences between female and male with major depression

G. Faludi, A. Sarosi, G. Balogh. *Semmelweis University Dept. of Psychiatry, Budapest, Hungary*

Epidemiologic data indicate that MD is approximately twice as common in women as in men. The biological hypotheses have been proposed to explain the predominance of MD in women attributes the sex difference in brain structure and function between men and women. Little is known about the effects of gender differences on cognition in depression. The objective of the study was to compare cognitive function between female and male patients suffering from DSM IV. major depressive episode. We hypothesized that both patient groups will show some gender-specific neurocognitive functioning. The neuropsychological battery included tests that assessed attention, verbal memory, non verbal memory, working memory, executive function. Results showed that females had better recalling memory as compared to men. There was a significant difference, males attained lower verbal memory scores as compared to females. While reproducing from memory the performance of both females and males was worse in comparison to normative data. When compared the colour identification period in patient group with the normative data obtained from generally accepted studies, it was observed that depressed group took a significantly longer period to identify colours. For measures visual scanning ability and speed attention there were significant differences between the patient group and standard subjects, women performed somewhat faster than men. The findings of this study suggest that although global cognitive impairment is absent in major depressive episode, deficit in most of the specific domains are present. Most individual test score differences were found within the memory and executive functioning domains, where depressed males typically were most impaired.

P-10-23

Mood disorders and their treatment in patients with epilepsy

C. Prueter, C. Norra. *Hospital Maria Hilf Psychiatry and Neurology, Gangelt, Germany*

Objective: Mood disorders in patients with epilepsy are frequently not diagnosed and not treated. Because of the high prevalence of depression and the resulting high suicide rate, precise diagnosis and effective therapy are very important.

Methods: A review of the literature is given

Results: Frequently, the clinical pictures of depressive syndromes in epileptics do not correspond with those described in operationalized classification systems such as ICD-10. or DSM IV. The incidence of depressive disorders in epileptics is estimated in the literature to be 30-70%. Multifactorial pathogenetic models include the type of seizures, the location of the epileptic focus, and neurotransmitter dysfunctions, as well as hereditary and psychosocial influences, and negative psychotropic effects of antiepileptic drugs (AEDs).

Conclusion: Despite an insufficient number of available controlled studies, based on the current data, treatment with the newer serotonergic antidepressants can be recommended for patients with epilepsy.Recommendations for therapy are given.

P-10-24

Comparison among measures of depression: Reliability, validity, relationship to anxiety and personality and the role of age and life events

K. N. Fountoulakis, P. Panagiotidis, S. Kaltartzis, M. Siamouli, A. Papadopoulou, M. Papadopoulou, S. G. Kaprinis, A. Iacovides. *3rd Dept. of Psychiatry Aristotle Univ Thessaloniki, Aretsou, Greece*

Objective: During the last decades, several scales assessing depressive symptoms emerged, however there are only a few studies comparing them in terms of reliability and validity.

Methods: The study sample included 40 depressed patients 29.65 ± 9.38 years old, and 120 normal comparison subjects 27.23 ± 10.62 years old. Clinical Diagnosis was reached by consensus of two examiners with the use of the SCAN v.2.0. The depressive scales applied and standardized were the CES-D, ZDRS, BDI-I, and the KSQ. Also, the STAI, the Life Events scale (Holms and Rahe), and the EPQ were administered. The analysis included the comparison of psychometric properties and the use of Pearson correlation coefficient and factor analysis.

Results: The results suggest that all scales correlated with anxiety measurements, sociodemographic variables, personality dimensions and non-significant indices to a similar extend. However, the MDI performed somewhat better, while the ZDRS had a very low internal consistency.

Conclusion: The comparison of several depressive scales provided no impressive results on the superiority or inferiority of a specific scale on the others.

P-10-25

Clinical, neurobiological and psychometric differences between early and late onset depressive illness

K.N. Fountoulakis. *Aretsou, Greece*

Tuesday, April 5, 2005

P-12. Poster session: Affective disorders II

Chairperson(s): Jules Angst (Zürich, Switzerland), Eduard Vieta (Barcelona, Spain)
11.15 - 12.15, Gasteig - Foyers

P-12-01

Olanzapine/fluoxetine and olanzapine treatment for bipolar depression: Open-label continuation in rapid cycling patients

S. Corya, P. Keck Jr., E. Vieta, J. Niswander, W. Xu, M. Tohen. *Eli Lilly and Company Lilly Research Laboratories, Indianapolis, USA*

Objective: Olanzapine/fluoxetine combination (OFC) has demonstrated efficacy in treatment of bipolar depression. This secondary analysis of patients with a history of rapid cycling (RC) examines the efficacy of OFC and olanzapine (OLZ) during a 6-month open-label (O-L) extension.

Methods: 833 subjects with an index depressive episode enrolled in an 8-week, double-blind, randomized trial with 315 RC patients receiving OFC (n=37), OLZ (n=140), or placebo (n=138). Patients achieving remission (MADRS≤8; YMRS≤12) entered O-

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L treatment receiving OLZ initially and switching to OFC any time after one week as needed.

Results: Compared to placebo and OLZ, mean change in total MADRS score revealed that OFC-treated RC patients improved significantly; 34.3% (12 of 35) achieved remission. During the O-L phase, 64.7% of RC (22 of 34) patients remained free from relapse (vs. 61.9% for non-RC patients). Mean time to relapse (MADRS≥16; YMRS≥15) into any mood episode was 141 days for rapid cyclers and 177 days for non-rapid cyclers. Mania relapse occurred in 12% of RC patients.

Conclusion: As management of depression is the primary unmet need in RC patients, OFC may represent an efficacious treatment for bipolar depression in patients with a history of rapid cycling.

P-12-02

A 24-week open-label extension study of olanzapine-fluoxetine combination and olanzapine monotherapy in the treatment of bipolar depression

S. Corya, D. Williamson, M. Case, D. Lin, M. Tohen. *Eli Lilly and Company Lilly Research Laboratories, Indianapolis, USA*

Objective: Olanzapine-fluoxetine combination (OFC) has shown efficacy in the acute treatment of depressive episodes in patients with bipolar I disorder. The present analyses examined the efficacy and safety of longer-term treatment with OFC or olanzapine monotherapy in a 6 month open-label extension study.

Methods: 376 patients with bipolar depression who completed an acute trial entered the open-label study and received 1 week of olanzapine monotherapy (5-20 mg/day). At all subsequent visits, patients could stay with olanzapine monotherapy (OLZ), or change to OFC (6/25, 12/25, or 12/50 mg/day). Three treatment groups were defined retrospectively according to the medication course taken from week 1: OLZ, OFC, or Switched. The efficacy measures were the MADRS, CGI, and YMRS.

Results: Among patients who started in remission, MADRS total scores did not change significantly from baseline to endpoint in the OFC (-0.7) or OLZ (1.4) groups, but increased slightly in the Switched (3.3, p=.02) group. For patients who started in non-remission, MADRS total scores decreased significantly in all groups (OFC -6.2, p<.001; OLZ –6.5, p=.003; Switched –4.4, p=.016). The majority of patients who entered the study in non-remission achieved remission (MADRS total score ≤12) during the trial (OFC: 66.7%, OLZ: 64.7%, Switched: 62.5%). The overall rate of depressive relapse was 27.4% and the overall incidence of mania emergence was 5.9%.

Conclusion: The present findings suggest that long-term treatment with olanzapine-fluoxetine combination is efficacious in the management of depressive symptoms and carries a low risk of mania emergence.

P-12-03

Safety and tolerability of quetiapine in bipolar mania

C. Adler, S. M. Strakowski, D. Fleck, M. Brecher. *Un. Cincinnati College of Med Department of Psychiatry, Cincinnati, Ohio, USA*

Objective: To review safety/tolerability in four placebo-controlled studies of quetiapine in bipolar mania.

Methods: Laboratory evaluations, adverse events, and Simpson Angus Scale (SAS) and Barnes Akathisia Rating Scale (BARS) scores were monitored in patients with bipolar I mania (DSM-IV) randomized to double-blind, placebo-controlled treatment with quetiapine (up to 800 mg/day) monotherapy (2 studies; 12 weeks) or in combination with lithium (0.7-1.0 mEq/L) or divalproex (50-100 mcg/mL) (2 studies; 3 or 6 weeks). The effect of quetiapine monotherapy on serum prolactin was also assessed.

Results: There were no clinically significant changes in laboratory tests, vital signs, weight, or ECG. Most adverse events were mild to moderate. Common adverse events (³10% and at least twice the placebo rate) with quetiapine monotherapy and combination therapy were somnolence and dry mouth. Treatment-related discontinuations due to adverse events were no different between quetiapine and placebo, nor was the incidence of extrapyramidal symptoms (including akathisia) (quetiapine monotherapy 12.9% vs placebo 13.1%; combination therapy 21.4% vs 19.2%). Mean change from baseline to treatment end in SAS and BARS scores was not significantly different between groups. Mean weight change (last observation carried forward) at treatment end was moderate: quetiapine monotherapy versus placebo +1.8 vs -0.15 kg; combination therapy +1.97 vs +0.27 kg. No patients withdrew due to weight gain. The effect of quetiapine monotherapy on serum prolactin levels was no different from placebo.

Conclusion: Quetiapine monotherapy and combination therapy are well tolerated in the treatment of bipolar mania. Supported by a grant from AstraZeneca.

P-12-04

Double-blind comparison of divalproex versus quetiapine monotherapy for adolescent patients with mania

C. Adler, M. DelBello, R. Kowatch, K. E. Stanford, J. Welge, D. Barzman, S. Strakowski. *Un. Cincinnati College of Med Department of Psychiatry, Cincinnati, Ohio, USA*

Objective: Determine whether quetiapine monotherapy is at least as effective (defined as at least 80% as effective) as divalproex for the treatment of adolescent mania.

Methods: Fifty adolescents (aged 12-18 years) with bipolar I disorder, manic or mixed episode, were randomized to quetiapine monotherapy or divalproex for 28 days.

Results: Twenty-five subjects were randomized to each treatment group. The mean (SD) decrease from baseline to endpoint in Young Mania Rating Scale (YMRS) score was 19.5 (2.4) in the divalproex group and 22.8 (2.4) in the quetiapine group. Based on the change in YMRS score in the divalproex group, we determined that the response in the quetiapine group needed to be within 4 points. The mean (SD) group difference in YMRS change from baseline to endpoint was 3.3 (3.4) (95% CI, -3.5, 10.1). Response rate for improvement in mania (Clinical Global Impression score </=2) was significantly greater in the quetiapine group than in the divalproex group (84% vs. 56%, p=0.03). There were no statistically significant group differences in rates of adverse events. The most common adverse event in both groups was sedation: quetiapine n=15 (60%) vs divalproex n=9 (36%, p=0.1).

Conclusion: Quetiapine is at least as efficacious as divalproex, and may be more efficacious than divalproex, in the treatment of adolescent patients with mania. Therefore, quetiapine may be used as monotherapy for the treatment of adolescent patients with mania. This research was supported by AstraZeneca.

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P-12-05

Efficacy of quetiapine in improving quality of life in patients with bipolar depression

J. Endicott, K. Rajagopalan, W. Macfadden, M. Minkwitz, J. Gaddy. *Columbia University NY State Psychiatric Institute, New York City, New York, USA*

Objective: Bipolar depression is associated with impaired quality of life (QOL). However, QOL has been under-investigated as a therapeutic target in bipolar disorder. This study investigated changes in quality of life in patients with bipolar depression treated with quetiapine.

Methods: Quetiapine monotherapy was studied in an 8-week, double-blind, placebo-controlled trial in patients with bipolar I or II disorder. Patients were randomized to receive quetiapine 600 mg/day (n=180), quetiapine 300 mg/day (n=181), or placebo (n=181). QOL was evaluated using the 16-item short form of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q SF) at baseline, Week 4, and Week 8.

Results: Baseline Q-LES-Q SF scores were low (quetiapine 600 mg/day group: 34.1; quetiapine 300 mg/day group: 36.1; placebo group: 34.2), consistent with poor HRQOL. At final assessment the improvement in Q-LES-Q SF score was significantly greater in both quetiapine treatment groups (11.7 in the 600 mg/day group and 10.8 in the 300 mg/day group) than in the placebo group (6.4, $p<0.001$). Significant improvement was noted at the first Q-LES-Q SF assessment (Week 4) in both quetiapine treatment groups versus placebo ($p<0.001$). Quetiapine was generally well tolerated, with low levels of extrapyramidal side effects and minimal weight gain.

Conclusion: Quetiapine monotherapy is effective in improving QOL in patients with bipolar depression. Supported by a grant from AstraZeneca.

P-12-06

Anti-anxiety effects of quetiapine in bipolar depression

W. Macfadden, J. R. Calabrese, R. McCoy, M. Minkwitz, E. Wilson, J. Mullen. *AstraZeneca, Wilmington, Delaware, USA*

Objective: Evaluate efficacy and safety of quetiapine monotherapy for anxiety symptoms in patients with bipolar depression.

Methods: 511 patients (342 bipolar I, 169 bipolar II depression) who received 8 weeks' double-blind treatment with quetiapine (300 or 600 mg/d) or placebo were included in the efficacy analysis. Symptoms of anxiety were assessed using the Hamilton Rating Scale for Anxiety (HAM-A).

Results: Mean baseline levels of anxiety measured by HAM-A score were similar across treatment groups: 18.6 to 18.9. Patients taking quetiapine 300 and 600 mg/d had significantly ($P<0.05$) greater improvement in mean HAM-A score vs placebo at every assessment starting with the first evaluation (Day 8) and sustained through endpoint (Week 8) (-8.6 and -8.7 vs -5.5). Common quetiapine adverse events (>/=10% and at least twice the placebo rate) were dry mouth (43%), sedation (31%), somnolence (26%), dizziness (20%), and constipation (11%).

Conclusion: Quetiapine monotherapy (300 or 600 mg/d) is significantly more effective than placebo for the treatment of anxiety symptoms in patients with bipolar depression. Quetiapine at doses of 300 or 600 mg/d was well tolerated in patients with bipolar depression. Supported by a grant from AstraZeneca.

P-12-07

Double-blind, placebo-controlled study of quetiapine in bipolar I depression

W. Macfadden, T. Suppes, J. R. Calabrese, R. McCoy, M. Minkwitz, E. Wilson, J. Mullen. *AstraZeneca, Wilmington, Delaware, USA*

Objective: To evaluate the efficacy and tolerability of quetiapine monotherapy for major depressive episodes in patients with bipolar I disorder.

Methods: Patients with bipolar I depression (N=360) were randomized to 8 weeks of double-blind treatment with quetiapine (fixed dose 600 or 300 mg/d) or placebo. The primary endpoint was change from baseline to endpoint in Montgomery-Asberg Depression Rating Scale (MADRS) total score.

Results: Patients taking quetiapine 600 or 300 mg/d had a significantly ($P<0.001$) greater improvement in mean MADRS scores vs placebo at every assessment, starting with the first evaluation (Week 1) and sustained through endpoint (Week 8) Significantly ($P<0.05$) more quetiapine patients (both doses) vs placebo were considered responders from Week 2 through the end of the study (Week 8) (>/=50% decrease from baseline MADRS score: 64% and 62% vs 33%). Treatment-emergent mania did not differ between quetiapine and placebo (3% vs 4%). Common quetiapine adverse events (³10% and at least twice the placebo rate) were dry mouth (42%), somnolence (32%), sedation (24%), dizziness (19%), and constipation (11%).

Conclusion: Quetiapine monotherapy (600 or 300 mg/d) is significantly more effective than placebo and well tolerated for the treatment of depressive episodes in patients with bipolar I disorder. Supported by a grant from AstraZeneca.

P-12-08

Mania remission rates and euthymia with quetiapine combination therapy

N. Sussman, J. Mullen, D. E. Sweitzer. *NYU Medical Center, New York, New York, USA*

Objective: Analyze rates of remission/euthymia in patients with bipolar mania receiving quetiapine and/or one other mood stabilizer.

Methods: A pooled analysis of two double-blind studies of patients hospitalized with bipolar I mania who received quetiapine (up to 800 mg/day) in combination with lithium (0.7-1.0 mEq/L) or divalproex (50-100 mcg/mL) for up to 6 weeks. Three different criteria of remission/euthymia were used to determine efficacy: (i) YMRS score of 12 or less; (ii) YMRS£12 plus a Montgomery-Asberg Depression Rating Scale (MADRS) score of 10 or less; and (iii) YMRS</=12 + MADRS</=8.

Results: Day 21 remission rates (YMRS</=12) were 48.7% (90/185) with quetiapine combination therapy versus 33.0% (61/185) with lithium or divalproex alone ($P=0.003$). Rates of euthymia (YMRS</=12 + MADRS</=10) were 43.2% (80/185) with quetiapine combination therapy versus 26.5% (49/185) lithium/divalproex alone ($P=0.001$). Using the more stringent criteria (YMRS</=12 + MADRS</=8) rates of euthymia of 38.4% (71/

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185) with quetiapine combination therapy versus 25.9% (48/185) for lithium/divalproex alone (P=0.014) were observed.

Conclusion: Quetiapine leads to sustained improvement in rates of clinical remission and euthymia. The benefit of quetiapine is similar regardless of the remission/euthymia criteria used. Supported by a grant from AstraZeneca.

P-12-09

Quetiapine for the treatment of rapid-cycling bipolar depression

E. Vieta, J. R. Calabrese, W. Macfadden, M. Minkwitz, J. Mullen. *University of Barcelona Hospital Clinic, Barcelona, Spain*

Objective: Depressive symptoms can be more severe and resistant to treatment in patients with rapid cycling bipolar disorder than in patients without rapid cycling. Evaluate the efficacy and tolerability of quetiapine monotherapy in the treatment of major depressive episodes in patients with bipolar disorder and a rapid-cycling disease course.

Methods: 108 patients with bipolar I or II disorder, rapid-cycling (DSM-IV), exhibiting moderate to severe depression who had been randomized to receive 8 weeks of double-blind treatment with fixed-dose quetiapine 600 mg/day (n=31), quetiapine 300 mg/day (n=42) or placebo (n=35) were included in the efficacy analysis. The primary endpoint was change from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) total score. Safety assessments included change from baseline in Young Mania Rating Scale (YMRS) total score.

Results: Patients treated with quetiapine (600 mg/day or 300 mg/day) had a significantly (P<0.01) greater improvement in mean MADRS score at every assessment, from Week 1 to Week 8, compared with placebo (-17.68, -18.57, -9.87, respectively). Minimal changes were noted on the YMRS throughout treatment, with no difference between-groups in mean change from baseline to Week 8 (+0.1, -1.1, -0.8). The number of patients who experienced treatment-emergent mania was low and similar in each group: quetiapine 600 mg/day (2), quetiapine 300 mg/day (2) or placebo (1). Common quetiapine adverse events were dry mouth, sedation, somnolence, constipation, and fatigue.

Conclusion: Quetiapine monotherapy (600 mg/day or 300 mg/day) is significantly more effective than placebo and is well tolerated for the treatment of patients with rapid-cycling bipolar depression. Supported by a grant from AstraZeneca.

P-12-10

Remission and response in the treatment of bipolar depression: Time-To-Event and NNT analyses from a large, randomized, controlled study of quetiapine

J. C. Cookson, P. E. Keck, Jr., T. A. Ketter, W. Macfadden, M. Minkwitz, J. Mullen. *City Mental Health NHS Trust, London, United Kingdom*

Objective: To evaluate the efficacy and safety/tolerability of quetiapine monotherapy in bipolar depression.

Methods: 542 patients with bipolar I or II disorder exhibiting moderate to severe depression were randomized to 8-weeks' double-blind treatment with quetiapine (600 or 300 mg/day) or placebo. Kaplan-Meier analysis and the log-rank, chi-squared test compared populations for time to response (>/=50% reduction from baseline in MADRS total score) and time to remission (MADRS total </=12).

Results: Mean time to response was significantly shorter with quetiapine 600 mg/day (25.50 days) and 300 mg/day (27.44 days) than placebo (37.05 days; log-rank chi-squared=30.73, df 2, P<0.001). Mean time to remission was also significantly shorter with quetiapine 600 mg/day (30.92 days) and 300 mg/day (33.22 days) compared with placebo (41.24 days; log-rank chi-squared=29.93, df 2, P<0.001). Response rates at Week 8 were 58% for both quetiapine dose groups and 36% for placebo (P<0.001). Remission rates were 53% for both quetiapine groups and 28% for placebo (P<0.001). NNT analyses similarly suggested efficacy of quetiapine (600 and 300 mg/day) compared with placebo (NNT=5 for both response and remission). Treatment-emergent mania was low and similar for quetiapine- and placebo-treated patients (3% vs 4%). Common quetiapine adverse events were dry mouth, sedation, somnolence, dizziness, and constipation.

Conclusion: Quetiapine (600 or 300 mg/day) significantly reduces time to response (by 31% and 26%, respectively) and remission (by 25% and 20%, respectively) compared with placebo, has favorable NNTs (5 for either dose for both response and remission), and is well tolerated. Supported by a grant from AstraZeneca.

P-12-11

Placebo-level eps and akathisia during quetiapine treatment for mania

B. Paulsson, H. Nasrallah. *AstraZeneca, Södertäje, Sweden*

Objective: Examine the incidence of EPS-related adverse events during treatment with quetiapine for bipolar mania.

Methods: Patients with bipolar I mania treated with quetiapine (up to 800 mg/d as monotherapy or in combination with lithium [0.7-1.0 mEq/L] or divalproex) in placebo-controlled, double-blind studies of up to 12 weeks' duration. Adverse event reports and Simpson-Angus Scale (SAS) and Barnes Akathisia Rating Scale (BARS) scores were outcome measures.

Results: EPS-related adverse events (including akathisia) with quetiapine monotherapy (12.9%) were no different than placebo (13.1%). Similarly, EPS-related adverse events with quetiapine plus lithium or divalproex (21.4%) were no different from lithium or divalproex monotherapy (19.2%). The incidence of akathisia was lower with quetiapine monotherapy than placebo (3.3% vs 6.1%), as it was with quetiapine combination therapy compared to lithium or divalproex monotherapy (3.6% vs 4.9%). No significant differences were observed between groups in SAS and BARS scores from baseline to endpoint. Anticholinergic use, a marker for EPS, was low in both groups.

Conclusion: The incidence of EPS (including akathisia) during quetiapine therapy for bipolar mania is no different from placebo. Avoiding EPS enhances the tolerability and acceptability of treatment, which is of particular importance for patients with bipolar disorder.

P-12-12

Quetiapine for agitation and aggression in bipolar mania

B. Paulsson, P. F. Buckley, M. Brecher. *AstraZeneca, Södertäje, Sweden*

Objective: To evaluate quetiapine for treating agitation and aggression associated with bipolar mania.

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Methods: The Positive and Negative Syndrome Scale (PANSS) Activation subscale, PANSS Supplemental Aggression Risk subscale scores, and the Young Mania Rating Scale (YMRS) were analyzed in patients with bipolar I disorder (manic episode, DSM-IV) treated with quetiapine (up to 800 mg/day) as monotherapy (two studies of 12 weeks duration) or in combination with lithium (0.7-1.0 mEq/L) or divalproex (50-100 mcg/mL) (3 or 6 weeks) in randomized, double-blind, placebo-controlled studies (Jones and Huizar. Bipolar Disord. 2003;5:57; Yatham et al. J Clin Psychopharmacol. 2004;24:599-606).

Results: Quetiapine monotherapy provided significantly greater improvements in the Activation and Supplemental Aggression Risk subscales of PANSS compared with placebo, with the difference by Day 21 and Day 84 being highly significant (P<0.001). This was supported by a significant improvement across all 11 items of the YMRS, including Disruptive/Aggressive Behavior (P</=0.001) and Irritability (P<0.001) at Days 21 and 84. There was no significant difference between groups in the PANSS Activation subscale scores at the end of combination therapy; however, significant improvements on the PANSS Supplemental Aggression Risk subscale were observed with quetiapine plus lithium or divalproex compared to lithium or divalproex alone at Day 21 (P<0.05). Quetiapine was well tolerated in all studies, with placebo-level EPS (including akathisia).

Conclusion: Quetiapine is clinically effective and well tolerated in the treatment of agitation and aggression in patients with bipolar disorder. The research presented was supported by funding from AstraZeneca.

P-12-13

Sustained remission/euthymia with quetiapine monotherapy for bipolar mania

B. Paulsson, T. A. Ketter, M. Jones. *AstraZeneca, Södertäje, Sweden*

Objective: Determine the effectiveness of quetiapine in bipolar mania using different criteria for clinical remission/euthymia.

Methods: Remission/euthymia following quetiapine monotherapy (up to 800 mg/day) or placebo (12-week, randomized, double-blind study) in patients hospitalized with bipolar I mania (Jones and Huizar. Bipolar Disord. 2003;5:57) were analyzed using three criteria: (i) Young Mania Rating Scale (YMRS) score </=12; (ii) YMRS </=12 plus a Montgomery-Asberg Depression Rating Scale (MADRS) score </=10; and (iii) YMRS </=12 plus MADRS </=8.

Results: Mean YMRS scores at entry were 33.3 (n=208) and 33.5 (n=195) in the quetiapine and placebo groups, respectively. After 3 weeks, remission/euthymia rates with quetiapine monotherapy versus placebo were: (i) 37.5% vs 23.1% (YMRS </=12); (ii) 35.6% vs 21.5% (YMRS </=12 plus MADRS </=10); and (iii) 35.1% vs 20.0% (YMRS </=12 plus MADRS </=8) (P<0.01). After 3 months, rates of remission/euthymia versus placebo were: (i) 65.4% vs 35.9% (YMRS </=12); (ii) 60.1% vs 30.8% (YMRS </=12 plus MADRS </=10); and (iii) 58.7% vs 29.7% (YMRS </=12 plus MADRS </=8) (P<0.001). Of the 37.5% (n=78) patients in remission/euthymia (YMRS </=12) after 3 weeks of quetiapine treatment, 89.7% maintained this status at 3 months. The average quetiapine dose in responders was 575 and 598 mg/day at 3 weeks and 3 months.

Conclusion: Quetiapine at a target dose of approximately 600 mg/day significantly improves the proportion of mania patients achieving clinical remission/euthymia, regardless of the assessment criteria used. Meaningful improvements with quetiapine monotherapy are sustained for at least 3 months. Supported by a grant from AstraZeneca.

P-12-14

Risperidone utilization in serious bipolar mood disorders

G. Tavormina. *Psychiatric Studies Centre, Provaglio d'Iseo (BS), Italy*

Objective: To assess Risperidone utilization and utility, and its safety and tolerability too, in serious bipolar spectrum mood disorders.

Methods: A total of 18 outpatients were included in this open-label, non-comparative, naturalistic study, meeting DSM-IV diagnostic criteria for bipolar mood disorders. These diseases were assessed: Bipolar Mood Disorder (type II), Bipolar Mood Disorder (type mixed), Cyclothymic Disorders. Risperidone treatment was a subsequent additional therapy to mood-stabilizers and antidepressants. "GAS" Scale was adopted in determining the effects of Risperidone treatment before beginning therapy, after eight weeks of mood-stabilizers and antidepressants therapy, and after six weeks of Risperidone treatment. Risperidone treatment was an additional therapy in combination with mood-stabilizers and antidepressants to obtain the optimum mood balance conditions. Tolerability was assessed by registering treatment-emergent adverse events.

Results: In beginning of therapy, all the patients obtained with the "GAS" a score lower than 35 points; after the eight weeks of therapy with mood-stabilizers and antidepressants the patients obtained with the "GAS" a score between 55 and 75 points. After the additional therapy with Risperidone, after others six weeks valuation, all the patients obtained with the "GAS" more than 85 points. TOLERABILITY - Only 17% of the patients had to stop the treatment, after the six weeks valuation, for not transient side effects (EPS; endocrine).

Conclusion: In this naturalistic study Risperidone demonstrated its considerable efficacy in serious bipolar spectrum mood disorder as add-on therapy to mood stabilizers and antidepressants, and also its safety and tolerability.

References

Akiskal HS. The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. J Clin Psychopharmacol 1996; 16 (suppl 1): 4-14.

Koukopulos A, Caliari B, Tundo A, Minnai G, Floris G, Reginaldi D, Tondo L. Rapid cyclers, temperament and antidepressants. Comp Psychiatry 1983; 24: 249-58.

Sachs GS. Bipolar mood disorder: practical strategies for acute and maintenance phase treatment. J Clin Psychopharmacol 1996; 16 (suppl 1): 32S-47S.

P-12-15

SSRI's during pregnancy: Do they really hurt the babies?

M. Steiner. *McMaster University, Hamilton, Canada*

Objectives: There are some reports that maternal use of selective serotonin reuptake inhibitor (SSRI) antidepressants in late pregnancy is associated with neonatal complications, and

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particularly respiratory distress; however, the quality of the available evidence is insufficient.

Methods: Outcomes of neonates whose mothers used SSRIs in late pregnancy (N=83), used SSRIs only in early pregnancy (N=36), or did not use SSRIs during pregnancy (N=137) were compared. All mothers were patients at a tertiary care reproductive mental health clinic. Data were abstracted from both maternal and infant hospital charts.

Results: No significant differences between groups were found in frequency of respiratory distress, tachycardia, admission to neonatal intensive care unit, or irritability. Birth weight differed significantly between the three groups ($p<0.05$), and post-hoc analysis revealed significant differences between infants exposed in early pregnancy (Mean wt.: 3286g) and unexposed infants (Mean wt.: 3527g); however, multiple regression revealed no effects of SSRI exposure after correction for gestational age. APGAR scores at one minute were significantly lower in infants exposed to SSRIs at term (Mean: 7.98) than control infants (Mean: 8.38, $p<0.05$). At five minutes, the difference between these two groups was no longer significant. The same pattern of results was observed when only mothers with significant symptoms of depression (Edinburgh Postnatal Depression Scale scores >11) were considered.

Conclusions: These findings are limited by a modest sample size and retrospective design. However, they do not support the existence of a neonatal withdrawal/discontinuation syndrome associated with maternal use of SSRIs in late pregnancy. Additional research is urgently required to aid decision making in treating pregnant women with depression.

Tuesday, April 5, 2005

P-15. Poster session: Affective disorders IV

Chairperson(s): Siegfried Kasper (Wien, Austria), Jean-Pierre Olie (Paris Cedex 14, France)
18.00 - 19.30, Gasteig - Foyers

P-15-01

Escitalopram in the treatment of severe depression

S. Kasper, P. Ninan, D. Ventura, J. Wang. *Medizinische Universität Allgem. Psychiatrie, Wien, Austria*

Objective: Escitalopram is the most selective serotonin reuptake inhibitor (SSRI) antidepressant, and has been shown to be more effective than citalopram, another SSRI, in the treatment of severe major depressive disorder (MDD). To determine prospectively the effect of escitalopram in the treatment of severe MDD.

Methods: Patients with severe MDD (mean baseline 24-item Hamilton Depression Rating Scale [HAMD] score=30) were randomly assigned to 8 weeks of double-blind treatment with 10-20 mg/day escitalopram (N=147) or placebo (N=153). Efficacy assessments included Montgomery-Åsberg Depression Rating Scale (MADRS; primary efficacy measure), HAMD, and Clinical Global Impression (CGI) scales. Response was prospectively defined in three ways: at least a 50% decrease in MADRS, or in HAMD total scores, or CGI-I <=2. Tolerability was assessed on the basis of adverse events (AEs).

Results: Overall, 82% of patients completed the trial. For LOCF analyses, escitalopram treatment led to significant ($p<0.05$) improvement versus placebo by week 2 in HAMD scores, and by week 4 in MADRS and CGI-I scores; statistically significant improvement compared with placebo was maintained at all subsequent visits. Approximately half of escitalopram treated patients (49-52%) at endpoint (LOCF) were responders, according to each definition, and these rates were significantly superior to placebo treatment (30-38%; $p<0.05$). Incidence of AEs was similar to those reported previously for escitalopram treatment. Discontinuation rates due to AEs were low (6% escitalopram, 0% placebo).

Conclusion: Escitalopram is an effective and well-tolerated treatment of severe major depression.

P-15-02

The efficacy and tolerability of escitalopram in depressed patients with or without concomitant anxiety

J.-P. Olie, B. Tonnoir, I. Florea. *Centre Hospitalier Sainte-Anne, Paris Cedex 14, France*

Objective: This was an open multicentre prospective study assessing the efficacy and tolerability of escitalopram in depressed patients with or without concomitant anxiety.

Methods: Escitalopram 10 to 20mg/day was administered over a 12-week treatment period in patients retrospectively divided into 3 groups according to their level of anxiety determined by HAM-A total score at baseline

Results: 649 out of 790 patients completed the study. At baseline, the mean MADRS total score was 31.5 (increasing as the HAM-A total score increased) and improved to 10.5 (OC) [12.4 (LOCF)] at endpoint. The mean HAM-A total score at baseline was 25.6, which improved to 9.0 (OC) [10.8 (LOCF)] at endpoint. There was no apparent effect on response to treatment of the presence or absence of anxiety, of the presence of one or more anxiety disorder at baseline, or of the type of anxiety disorder present. However, the therapeutic effect on anxiety (assessed by HAM-A) was slightly increased, while the therapeutic effect on depressive symptoms (assessed by MADRS) was slightly reduced, when either the severity of baseline anxiety or the number of comorbid anxiety disorders were high, suggesting a strong anxiolytic effect. 251 patients (32%) had adverse events (AEs). The AEs that occurred most frequently were nausea in 67 patients (8%) and headache in 38 patients (5%); 61 patients (8%) discontinued due to AEs.

Conclusion: Escitalopram was effective at reducing symptoms of depression in patients with or without comorbid anxiety over the 12-week treatment period and was well tolerated.

P-15-03

A comparison of escitalopram and mirtazapine and placebo in driving performance, psychomotor performance and cognitive function in healthy subjects

S. Langer, M. Wingen, H. Andersen, J. Bothmer, J. Ramaekers. *Lundbeck GmbH Clinical Research, Hamburg, Germany*

Objective: Some antidepressant drugs are known to produce side effects like drowsiness and sedation, which may impair psychomotor functioning. Consequently, antidepressants may have an impact on everyday safety, including driving. The objective of this study was to evaluate the effect of escitalopram (10-20mg/day) and mirtazapine (30-45mg/day) in healthy subjects, primarily on driving performance

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