P01.18

Antidepressants of the different chemical groups: clinical and neurophysiological correlations in treating depression

E. Grigorieva*, A. Dyakonov. *Yaroslavl State Medical Academy, Department of Psychiatry, Russia*

Developing options of the psychopharmacology require specialists to conduct goal-oriented and adequate therapy.

The objective of the research was a comparative clinical and neurophysiological study of the action of amytriptyline, tyaneptine, fluoxetine and moclobemide, treating depressive disorders with the dominant affect of anguish.

Totally, 107 depressed patients, aged 20–40, with depressive episode (38,3%), recurrent (53,3%) and bipolar (8,4%) affective disorders were clinically examined. Depression severity was assessed by clinical examination as well as by the administration of HAM-D Rating Scale and CGI Scale prior to and on the 10th, 20th and 40th days of treatment. Brain-wave mapping was recorded before the therapy and on its 20th day. All patients were divided onto 4 groups: those, who were treated with amytriptyline (n=25), tyaneptine (n=28), fluoxetine (n=32) and moclobemide (n=22). Daily dosages of amytriptyline (150–250 mg), tyaneptine (37.5–50 mg), fluoxetine (40–60 mg) and moclobemide (450–600 mg) depended on the depression severity (moderate or severe levels). Control group consisted of 25 healthy people.

Results of the study showed: when registering brain bio-electric activity of depressed patients prior to the treatment in comparison with the healthy group we have observed zones of "increased" activity in the right temporal fields and zones of "decreased" activity in the left temporal fields. Changes, occurring in these zones in response to the treatment, were more stable. Affecting the brain electric impulses all used agents demonstrated a similarity (core pattern) as well as the differences. All antidepressants reduced the activation of the right temporal zone and increased the activation of the left temporal zone. As a specific feature of the action, fluoxetine and moclobemide produced more significant increasing of the left temporal zone's activation. Amytriptyline caused an expanding of the activation zone from the left temporal fields to parietal and occipital fields. Tyaneptine produced migrating zones of activation.

P02. Antipsychotics

P02.01

Coadministration of clozapine and amisulpride in psychotic patients

M. Ziegenbein*, O. Rosenthal, P. Garlipp. *Hannover Medical School, Department of Psychiatry, Germany*

Clozapine was the first atypical antipsychotic drug to be introduced into clinical use in several European countries. Clozapine treatment is associated with wide side-effects. The mechanisms underlying these side effects are still unknown. The wide side-effects are very often responsible for substantial compliance problems. Previous case reports have shown before that the coadministration of amisulpride and clozapine might be useful to reduce side-effects. We performed an open clinical study to gather more experience in the clinical effiency of the coadministration of the two drugs. Nine psychotic inpatients (6 female, 3 male; mean age 42,8 [plusminus] 12,3) participated and were diagnosed according to DSM-IV criteria. The clozapine treatment was associated with side-effects and persisting psychotic symptoms. Under addition of amisulpride we found very low dosages of clozapine to be sufficient to obtain effective clozapine concentrations. Secondly, we found a low incidence of side effects. All patients were in clinical remission. Our results indicate that amisulpride addition to clozapine is highly effective in reducing psychotic symtomatology and side-effects. This might be due to additive effects of the two drugs and/or metabolic interaction.

P02.02

Characteristics of acute schizophrenic patients on atypical antipsychotics

V.P. Kontaxakis*, B.J. Havaki-Kontaxaki, C.T. Kollias, M.M. Margariti, S.S. Stamouli, G.N. Christodoulou. *Department of Psychiatry, University of Athens, Eginition Hospital, Athens, Greece*

Objective: The aim of this study is to reveal the differential characteristics of acute schizophrenic inpatients on atypical antipsychoties.

Methods: The subjects of this study were sixty-three schizophrenic patients consecutively admitted at Eginition Hospital, Athens. All patients were assessed on admission using the Positive and Negative Syndrome Scale (PANSS). Patients' case notes analysis was performed surveying antipsychotic drugs' prescribing on the first week after their admission. Twenty-two patients were on atypical antipsychotics and forty-one patients were on conventional antipsychotics. Patients on atypical antipsychotics (AA) were compared with those on conventional antipsychotics (CA) in many social-demographic, clinical and psychopathological parameters. **Results:** There were no statistically significant differences between schizophrenic patients on AA and those on CA regarding age, sex, family status, employment status, duration of illness, PANSS-total score, PANSS- positive subscale score, PANSS-negative subscale score, PANSS-general psychopathology subscale score. Schizophrenic patients on AA scored lower on the item G14 of the PANSS (poor impulse control, 1.5 vs 2.2, U=168, p=0.08, statistically significant trend).

Conclusion: Acute schizophrenic inpatients on atypical antipsychotics were differentiated from those on conventional antipsychotics in that they had a better impulse control.

P02.03

Cognitive function in stable outpatients switched to ziprasidone

P.D. Harvey[1], H.Y. Meltzer[2], S.J. Romano[3]. [1]*Mount Sinai School of Medicine, New York;* [2]*Psychiatric Hospital at Vanderbilt, Vanderbilt University Medical Center;* [3]*Pfizer, Inc., New York, USA*

Objectives: To assess cognitive function were assessed in stable outpatients switched to ziprasidone from conventional or other novel antipsychotic agents.

Methods: 3 separate, 6-week multicenter trials assessed the effects of switching patients from conventional antipsychotics (n=108), olanzapine (n=104), or risperidone (n=58) to ziprasidone. Patients were randomly switched to ziprasidone 40–160 mg/day by 1 of 3 schedules for discontinuing their previous medication. Just before switching, and weekly during ziprasidone treatment, they were evaluated using a battery of assessments of working and secondary memory, vigilance, visuo-motor speed, verbal fluency, and executive functioning.

Results: Patients switched to ziprasidone manifested wide-ranging improvements in cognitive function. Significant ($P<0.05$ by ANCOVA) improvements were seen at endpoint (LOCF) in memory, vigilance (in patients switched from conventional antipsychotics or risperidone), executive function (in patients switched from conventional antipsychotics or risperidone), and verbal fluency.

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Conclusions: These findings suggest that patients requiring a change in antipsychotic therapy may experience cognitive improvements following a switch to ziprasidone.

P02.04

Ziprasidone vs olanzapine for cognitive function in schizophrenia

P.D. Harvey[1], G. Simpson[2], R. Horne[3], P.J. Weiden[4], M. Bari[5], S.J. Romano[6]. [1]*Mount Sinai School of Medicine, New York;* [2]*LAC & USC Medical Center, Los Angeles;* [3]*Lake Mead Hospital, Las Vegas;* [4]*SUNY Health Sciences Center, Brooklyn;* [5]*Synergy Clinical Research Center, Crula Vista;* [6]*Pfizer, Inc., New York, USA*

Objective: To compare cognitive changes in patients treated with ziprasidone versus olanzapine.

Methods: Patients with schizophrenia or schizoaffective disorder were randomly assigned to 6 weeks' double-blind therapy with olanzapine (n=133) or ziprasidone (n=136) therapy. Cognitive tests – at baseline and end of week 6 or early termination – included measures of vigilance, executive functioning, verbal learning and memory, verbal fluency, and visuo-motor speed. Endpoint data were available for at least 49 ziprasidone patients and 60 olanzapine patients (numbers varied by test administered).

Results: There were statistically significant improvements from baseline for both groups in vigilance, visuo-motor speed, verbal learning and delayed recall, and category fluency, but no improvements in letter fluency or executive functioning. Olanzapine patients had statistically greater improvement (p=0.015) in category fluency, a finding that would not have withstood correction for overall number of tests performed.

Conclusions: Ziprasidone exerts a beneficial effect on several domains of cognition known to affect functional outcome in schizophrenia. Few notable differences were detected between ziprasidone and olanzapine, suggesting that ziprasidone has cognition-enhancing effects similar to those of other newer antipsychotics.

P02.05

Health status indices in stable outpatients switched to ziprasidone

P.J. Weiden[1]*, D.G. Daniel[2], G. Simpson[3], S.J. Romano[4]. [1]*SUNY Health Sciences Center, Brooklyn;* [2]*Comprehensive Neuroscience, Inc., Falls Church;* [3]*LAC & USC Medical Center, Los Angeles;* [4]*Pfizer, Inc., New York, USA*

Objective: To assess ziprasidone's impact on health indices in outpatients switched from other antipsychotics.

Methods: Stable, symptomatic outpatients with schizophrenia were switched to ziprasidone (40–160 mg/day) from conventional antipsychotics (n=108), olanzapine (n=104), or risperidone (n=58) in 3 identical, 6-week, open-label trials, using random assignment to 1 of 3 crossover strategies. Primary outcome was mean change from baseline to endpoint in total cholesterol, triglycerides, prolactin (nonfasting); weight and BMI; and movement disorders.

Results: Patients switched from olanzapine experienced significant mean weight loss (–3.5 lb; P<0.001) and BMI (P<0.0001). Significant improvements in total cholesterol and triglycerides occurred in patients switched from olanzapine (P<0.0001) and risperidone (P<0.01). Significant decreases in prolactin occurred in patients switched from conventional antipsychotics (P=0.05) and risperidone (P<0.0001). Movement disorders were infrequent with ziprasidone, with significant improvement noted after switch from conventional antipsychotics (P<0.0001) and risperidone (P<0.01). Ziprasidone was well tolerated, with discontinuations from AEs ranging from 6–11%.

Conclusions: Switching to ziprasidone from conventional antipsychotics, olanzapine, or risperidone resulted in significant improvement in several important indices of health status.

P02.06

Therapeutic response in stable outpatients switched to ziprasidone

P.J. Weiden[1]*, G. Simpson[2], S.G. Potkin[3], S.J. Romano[4]. [1]*SUNY Health Sciences Center, Brooklyn;* [2]*LAC & USC Medical Center, Los Angeles;* [3]*University of California, Irvine;* [4]*Pfizer, Inc., New York, USA*

Objectives: To determine the influence of previous maintenance antipsychotic therapy and speed of cross-taper technique on post-switch efficacy and tolerability of ziprasidone in outpatients with schizophrenia.

Methods: Three identical, 6-week, open-label, randomized trials were conducted in stable, symptomatic outpatients with schizophrenia switched to ziprasidone (40–160 mg/day) from conventional agents (n=108), olanzapine (n=104), or risperidone (n=58). Subjects were randomized to one of three cross-taper schedules – fast, slow, or abrupt discontinuation – for week 1 on ziprasidone. Baseline and outcome assessments included PANSS and CGI-S.

Results: All three crossover schedules were well tolerated, showing no outcome differences by crossover method. Significant symptom improvement from baseline occurred in total PANSS and CGI-I in all three studies. Prior antipsychotic medication did not influence degree of improvement seen.

Conclusions: Stable but symptomatic outpatients switched from other first-line antipsychotics to ziprasidone usually found ziprasidone to be tolerable and effective. Most patients showed symptom improvements within the 6-week treatment period, whether they were switched from conventional or first-line atypical antipsychotics. These results indicate that many patients will experience clinical improvements after being switched to ziprasidone.

P02.07

Ziprasidone vs haloperidol for IM/oral therapy of acute schizophrenia

S. Brook[1]*, W. Jorge[2], I. Benattia[3]. [1]*Sterkfontein Hospital, South Africa*
[2]*University of Freiburg, Germany*
[3]*Pfizer, Inc., New York, USA*

Objectives: To compare efficacy and tolerability of sequential IM/oral ziprasidone versus haloperidol in acute schizophrenia.

Methods: 6-week flexible-dose, randomized trial of ziprasidone (<40 mg IM, 80–160 mg oral; n=429) and haloperidol (<10 mg/day IM, 5–20 mg/day oral; n=138). Primary outcomes (change from baseline: BPRS, CGI-S, CGI-I. Secondary outcomes (assessed throughout): Covi, ESRS, BAS, AEs.

Results: Change in BPRS total was significant for ziprasidone versus haloperidol at visit 1 (P<0.005), comparable thereafter. Endpoint CGI-S, frequency distribution of CGI-I, and change in BPRS anxiety scores were comparable throughout. CGI-I scores were "much" or "minimally" improved for most patients, with significantly more ziprasidone completers responding on visits 1 (P<0.05) and 2 (P<0.01). Haloperidol patients had greater mean change from baseline BAS and ESRS scores at all visits (both P<0.0001). Treatment-emergent AEs in >10% of patients included anxiety, insomnia, somnolence – ziprasidone; and akathisia, dystonia, EPS, hypertonia, tremor, insomnia – haloperidol.

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