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Satellite Symposia

Zeneca Pharmaceuticals

ST1. From receptor to outcome: the impact of atypical antipsychotics in schizophrenia

Chairman: T Burns

Abstracts not received.

Eli Lilly and Company

ST2. Outcomes of treatment of schizophrenia

Chairman: N Sartorius

IMPACT OF TREATMENT ON THE CORE DEFICIT PATHOLOGY

William T. Carpenter, Jr. *Maryland Psychiatric Research Center, Baltimore, Maryland*

Negative symptoms define one of the three core domains of psychopathology of schizophrenia and account for much of the long-term morbidity. Treatment is crucial, but the issues are complex.

Most patients with schizophrenia manifest negative symptoms, but the core deficit pathology is only present in a subgroup. Therefore, the first step in treatment is a differential diagnosis of the negative symptoms. For example, anhedonia may be secondary to depression; social withdrawal may be secondary to psychosis or paranoid guardedness; anergia or restricted affect may be secondary to neuroleptic treatment; or alogia may be secondary to low stimulation in the interpersonal environmental. Each of these secondary causes of negative symptoms has direct treatment implications.

More difficult to treat are negative symptom manifestations of the enduring trait referred to as schizophrenia deficit pathology. Clinical trials have rarely isolated these primary negative symptoms for treatment efficacy assessment. This has been done in two studies of clozapine, and it was found that the superior antipsychotic efficacy extended secondary, but not to primary, negative symptoms.

The clinical trials design required to evaluate treatment of deficit pathology will be described, and the status of pharmacologic and psychosocial therapies will be reviewed.

EFFECTS OF ACUTE TARDIVE EPS ON OUTCOME

Jes Gerlach. *St. Hans Hospital Roskilde, Denmark*

Extrapyramidal side effects (EPS), especially akathisia, dystonia, parkinsonism and dyskinesia, are seen in up to 90% of neuroleptic-treated patients with schizophrenia. Each syndrome may occur as a separate entity or may be concurrent with other syndromes. They may be acute or tardive, reversible or irreversible and with or without subjective distress. These EPS represent a severe draw-back in an otherwise useful antipsychotic therapy. They may be distressing and disabling, e.g. by causing muscle tension, slow movements and restlessness-anxiety (akathisia) which sometimes counteract the antipsychotic effects. EPS are a major cause of poor compliance with treatment which in turn leads to relapse, rehospitalization and morbidity. Furthermore, EPS cause suffering for relatives, limit possibilities for rehabilitation and leisure activities, and deter social integration. The most severe complications are the irreversible tardive syndromes such as tardive dyskinesia and tardive dystonia. These may ruin the life of a psychotic patient and be clearly worse than the psychotic condition.

With this background it is important for physicians and nurses to become more aware of EPS, being able to recognize EPS in discrete forms and at early stages, and become better trained in their prevention and proper management. The use of the lowest effective dose strategy and new antipsychotics with low dopamine receptor blocking effect are important means in this respect.

EFFECT OF NON-PHARMACOLOGIC INTERVENTIONS ON OUTCOMES

Kimberly Littrell. *APRN, Promedica, Inc., Tucker, Georgia*

During the past decade a dramatic paradigm shift has occurred related to the treatment of schizophrenia. Enhanced understanding of brain pathophysiology along with the introduction of more efficacious antipsychotic agents has led to dramatic improvements in the condition of people with schizophrenia. These improvements, while gratifying and exciting, have challenged treatment providers to improve the quality of non-pharmacological interventions. Professionals who had previously focused on maintenance and stability are now called to implement innovations in their clinical practice which elevate their patients to a higher level of functioning. While it appears evident that improved patient outcomes lie within the combined strategies of pharmacotherapy and psychosocial interventions, little attention has been paid to the latter.

Non-pharmacological interventions may be broadly classified into the areas of psychotherapy, psychoeducation, psychosocial/skills training, and medication management. Psychotherapy, both the individual and group format, provides a rich opportunity for the person with schizophrenia to process their experience of the illness and reconnect with others in a non-psychotic manner. With diminished symptoms and improved cognitive functioning, individuals are now able to effectively engage and benefit from psychoeducational strategies. These strategies should, however, be dynamic in nature and reflect the natural evolution of the recovery and reintegration process. Psychosocial interventions and skills training should focus on establishing and maintaining relationships with peers in a non-institutional, commu-

nity setting. Medication management poses a particular challenge with the new antipsychotic medications, as all are available only in oral formulation. This raises issues of compliance and the ability to adhere to long-term maintenance pharmacotherapy.

Attention should also be given to individual's subjective experience of the illness and recovery. What questions and concerns does this person have? Issues of fear, apprehension, anxiety, excitement, and loneliness have been documented. How treatment professionals respond to these issues may have strong impact on the course of the individual's recovery. Engagement of the family and/or other caregivers is another important non-pharmacological intervention. As family members are still the primary care provider for adults with schizophrenia, their knowledge, availability, and involvement are crucial areas for assessment.

Outcome measurements must be interwoven with the actual healthcare delivery. Multidimensional measurements which address issues of psychopathology, social adjustment, role functioning, quality of life, violence/suicidality, family burden, patient satisfaction, and hope are examples of assessment areas.

Videotape of case examples will be presented to better illustrate effective non-pharmacological strategies when working with adults with schizophrenia.

IMPACT OF OLANZAPINE ON QUALITY OF LIFE IN SCHIZOPHRENIA

Christophe Martin. *Lilly Research Center, Windlesham, Surrey, UK*

There is greater recognition that alleviation of the psychopathology of schizophrenia and other psychotic disorders only addresses part of the problems experienced by these patients, and that comprehensive evaluations of new antipsychotic drugs require both clinical and quality of life outcome assessments. Olanzapine (Olz), a thienobenzodiazepine, is a putative new "atypical" antipsychotic agent that has been shown to be effective and well-tolerated in the treatment of schizophrenia. In a double-blind clinical trial conducted in 174 academic and community centers in 17 countries, 1,996 patients with schizophrenia, schizophreniform disorder or schizoaffective disorder were randomized to either Olz (5–20) mg/day; n = 1,336) or haloperidol (Hal) (5–20 mg/day; n = 660). BPRS total scores, PANSS positive and negative scores, CGI severity scores, and Quality of Life Scale (QLS) total and subscale scores were measured at baseline, after 6 weeks of treatment, and over a treatment period of 52 weeks for patients who responded to 6 weeks of acute therapy. All patients with a baseline and at least one postbaseline QLS assessment (Olz: 636; Hal: 257 patients) were included in the quality of life analyses. During the acute treatment phase, mean improvements in BPRS total, PANSS negative, CGI severity, and QLS total scores were statistically significantly greater in the Olz group compared to the Hal group. The greater improvements in quality of life scores were maintained over the 52-week treatment period and appeared to be due to a more pronounced impact of olanzapine on intrapsychic foundations, a measure of patient sense of purpose, motivation and emotional interaction.

In conclusion olanzapine was effective and superior to haloperidol in improving quality of life in patients with schizophrenia and related psychotic disorders.

BIOLOGICAL AND SOCIAL PREDICTIONS OF OUTCOME IN PSYCHOSIS

R.M. Murray. *Department of Psychological Medicine, Institute of Psychiatry de Crespigny Park, London SE5 8AF*

A series of 166 psychotic patients was extensively investigated and followed up for 4 years. Among schizophrenic patients, males had an earlier onset of psychosis than females, but this difference disappeared when patients who had suffered obstetric complications were removed. Ventricular volume did not differ among female schizophrenics with or without a family history, but non-familial male schizophrenics had greater ventricular volume than familial cases; this was not explained by obstetric complications.

Male patients had a poor outcome while patients who had suffered adverse life events had a good outcome. Early insidious onset, low IQ, and childhood problems were bad prognostic indicators as was increased Sylvian fissure and third ventricular volume.

Wyeth-Ayerst International

ST3. The evolving role of venlafaxine: a dual action antidepressant

Chairman: C de Montigny

THE SYNERGISTIC BENEFITS OF SEROTONIN AND NORADRENALINE REUPTAKE INHIBITION

J. Craig Nelson. *Professor of Psychiatry, Department of Psychiatry, Yale University School of Medicine, 20 York Street, New Haven, Connecticut 06505*

The recent success of the SSRIs has underscored the importance of serotonin in the pathophysiology of depression. Yet, norepinepherine and serotonin both appear to play important roles in mediating antidepressant response. Tryptophan depletion studies have demonstrated that serotonergic antidepressants are dependent on serotonin for their efficacy, but that blocking serotonin synthesis has little effect on the efficacy of noradrenergic antidepressants, such as desipramine. Alternatively, administration of alpha-methyl-paratyrosine, a drug inhibiting catecholamine synthesis, causes relapse in patients successfully treated with desipramine, but not serotonergic antidepressants. The findings suggest both neurotransmitters provide alternative pathways mediating antidepressant response. Preclinical work suggests the combination of drugs acting on both systems may enhance neuropharmacologic changes. Based on these preclinical findings, we conducted a preliminary study comparing the combination of desipramine and fluoxetine to desipramine alone in a group of severely depressed inpatients. The combination was more rapidly effective, with differences noted after one and two weeks. At the end of four weeks, more patients had responded to the combination. While this was an open study, the data suggested the combination of a serotonergic and noradrenergic drug enhanced efficacy. Recent drug development has focused on the possible benefits of drugs with combined action. Venlafaxine, a new SNRI antidepressant, has both serotonergic and noradrenergic effects. Clinical studies suggest it is more effective than selective drugs in severely ill patients.

EXPANDING APPLICATIONS FOR VENLAFAXINE, A DUAL ACTION ANTIDEPRESSANT IN CLINICAL MEDICINE

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In addition to their use in depression, there is growing interest among researchers and clinicians in a variety of new indications for antidepressants. Future clinical trials of venlafaxine, a new

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