LS-04-02

Drug abuse and bipolar disorder

S. Stakowski. *Germany*

In the 1920s, Kraepelin recognized the frequent occurrence of alcoholism in bipolar disorder. The incidence of comorbid alcohol and substance abuse with bipolar disorder ranges from 46%-76% compared to only 14% in the population as a whole. Thirty-four percent of bipolar patients with a history of suicide attempts have a positive family history of drug abuse. Alcoholism appears to be more prevalent in family members of bipolar adults and children. The severity of mania episodes, but not depressive episodes, is associated with drug abuse. Substance abuse is associated with medication non-compliance, more mixed or dysphoric mania, and more hospitalizations. Correct diagnosis needs to be a priority since drugs of abuse, particularly stimulants are associated with symptoms similar to those of mania or even psychosis.

LS-04-03

Depression and bipolar disorder

H.-J. Möller. *Ludwig-Maximilians-Universität Klinik für Psychiatrie, München, Germany*

Bipolar depression is difficult to diagnose and challenging to treat. Sixty percent of patients are misdiagnosed an average of 3.5 times before receiving the appropriate diagnosis. Most commonly, patients are misdiagnosed as having unipolar depression, anxiety disorder, and schizophrenia. Methods of distinguishing bipolar depression from other psychiatric illnesses will be presented. Past history, phenomenology, family history, and treatment response will all be characterized as indicators of the presence of bipolar disorder. Differential diagnosis is imperative in choosing therapy. One focus will be the available treatment options, as well as the appropriate use of antidepressants.

Monday, April 4, 2005

LS-02. Satellite symposium: Antidepressant myths and facts: Do the data reflect clinical reality?

Supported by an unrestricted educational grant from Pfizer Inc.

Chairperson(s): David Sheehan (Tampa, USA)
12.30 - 14.00, Gasteig - Philharmonie

Chair's introduction

D. Sheehan. *University of South Florida College of Medicine, Tampa, USA*

LS-02-01

Diagnosis and treatment of spectrum depression and anxiety disorders

G. Cassano. *University of Pisa Dept. of Psychiatry,Neurobiol., Pisa, Italy*

Diagnosis of psychiatric disorders is made according to fulfilment of the criteria defined by the current editions of the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) or the International Classification of Diseases (ICD). While there is no doubt that these categorical diagnostic tools are simple and reliable, they have their limitations, since the symptomatology and response to treatment varies between patients. Failure to recognize and manage residual, comorbid, or subthreshold spectrum features may explain continued impairment, even when the core condition has been well treated. An alternative approach, which may better capture an individual's condition, may be the consideration of a 'spectrum' of psychiatric illness. This would encompass various psychiatric symptoms from depression to anxiety, somatic symptoms such as pain, personality traits, and behavioural features related to an established DSM-IV disorder construct. Unexplained somatic symptoms, such as headache and bodily weakness, play an important role in the manifestation of mood disorders. Unfortunately, painful physical symptoms are usually rarely detected. This spectrum approach to diagnosis could be used to optimize management strategies and monitor the course of illness. Community patients presenting with panic disorder, social phobia, or generalized anxiety disorder (GAD) have high rates of lifetime depression comorbidity of approximately 50%. Psychiatric comorbidity is frequent in all age groups, and is associated with increased severity of illness, poor social function, increased somatic symptoms, and greater suicidality. It is also linked to poor treatment outcome, possibly resulting from delayed or diminished response to treatment, or reduced compliance. Although highly prevalent, comorbid depression and anxiety is underdiagnosed and undertreated despite the availability of effective therapies. There is therefore a need to raise awareness among physicians to ensure optimal treatment for patients, and to overcome public misconceptions regarding psychiatric disorders and medications. Clinical trials of antidepressant efficacy in anxiety or depression often exclude patients with psychiatric comorbidity. This presentation will review recent studies demonstrating the efficacy of selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs) in patients with a variety of comorbid psychiatric disorders, including major depressive disorder comorbid with panic disorder, obsessive-compulsive disorder, or GAD. Data regarding efficacy in post-traumatic stress disorder (PTSD) comorbid with depression or anxiety, and in anxious depression, will also be considered. These studies indicate that some antidepressants are as effective and well tolerated in patients with psychiatric comorbidity as in single mood and anxiety disorders. In summary, this presentation will explore the use of a spectrum model for diagnosis, consider the particular challenges of diagnosis and treatment of psychiatric comorbidity, and review clinical study data evaluating the efficacy of antidepressants in treating patients with comorbid psychiatric disorders.

LS-02-02

The importance of actively treating depression in medically ill patients

R. Krishnan. *Duke University Dept. of Psychiatry, Durham, USA*

Depression occurs at a considerably higher rate in patients with medical illness compared with healthy individuals; its prevalence ranges from 10% to 50% in medically ill patients. Comorbid depression is associated with greater physical impairment and with

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poor treatment compliance, negatively impacting upon recovery and outcome. These factors pose a risk to morbidity and mortality, and increase the economic and healthcare burden of medical illness, thus providing a rationale for actively treating depression in medically ill patients. There is evidence that in patients with ischemic heart disease, or vascular conditions such as stroke, comorbid depression increases medical mortality, and a number of proposed mechanisms for this relationship will be briefly reviewed. For example, enhanced platelet activation/aggregation and reduced heart rate variability in depressed patients may be associated with cardiac illness. The benefits of treating depression in medical illness have been studied only to a limited extent. There has previously been a reluctance to use antidepressants in medically ill patients, possibly because of their frailty and potential safety concerns. It may also be that depression in medically ill patients is seen as understandable and therefore not in need of treatment. However, several recent studies show that antidepressants are safe and efficacious in this population. This presentation will review existing and emerging data from antidepressant studies in patients with a range of comorbid medical illnesses. Initial pilot studies suggested that selective serotonin reuptake inhibitors (SSRIs) could be used safely in patients with ischemic heart disease, although efficacy outcomes were less conclusive. The Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) was the first large, double-blind study of depression in post myocardial infarction patients. This 24-week study clearly demonstrated that sertraline is a safe treatment for comorbid depression in this patient population, with no adverse cardiovascular effects. Sertraline treatment was also associated with benefits regarding depressive symptoms and a reduction in platelet/endothelial activation, a potential advantage in these patients. Controlled studies demonstrating benefits of SSRI treatment for depression comorbid with other medical illnesses will be reviewed, including post-stroke, diabetes, chest pain of unexplained etiology, and Alzheimer's disease. There are significant benefits in actively treating depression in medically ill patients, and certain antidepressants can be used safely in this patient population. However, antidepressants should be evaluated on an individual basis to determine their efficacy and safety in medically ill patients. This patient population is also likely to be taking multiple medications, therefore the potential for drug-drug interactions should be taken into account when selecting treatment.

LS-02-03

First and second line antidepressants: Evidence-based considerations

D. Sheehan. *University of South Florida College of Medicine, Tampa, USA*

Are the theoretical differences in antidepressant mode of action associated with differences in therapeutic effect or side effects in clinical practice? Which is better in terms of efficacy and safety: selectivity or multiple sites of action? A number of double-blind, placebo-controlled studies, and pooled analyses comparing selective compounds (such as SSRIs) and agents with more than one mode of action (for example, some TCAs, SNRIs) suggest that there are no significant differences in efficacy,1,2 but there may be significant differences in safety and tolerability. These factors should be considered when defining first- and second-line treatments. However, these findings are still debated. Comparison of data from different randomized, controlled clinical trials (RCTs) is difficult due to variations between trials. Recently, meta-analyses, or pooled analyses, have become important tools for the evaluation of clinical trial data in order to increase the size of the patient cohort and therefore the statistical power of RCTs; however, the results are only as rigorous as the criteria for selecting the studies. Careful evaluation of the study design, outcome measures, and statistical methods should be carried out to ensure that the study conclusions are fully supported by the data. The drawbacks to these methods will be discussed, and the validity and clinical meaning of recent meta-analyses and RCTs comparing SSRIs and SNRIs will be critically evaluated. Although SSRIs and SNRIs show similar efficacy in depression and anxiety, tolerability and safety should also be a major consideration. Evidence suggests that certain SNRIs are associated with high levels of discontinuation-emergent adverse events, and that norepinephrine reuptake inhibitors are associated with hypertension and other cardiovascular risks. RCTs and a meta-analysis have indicated that venlafaxine has a dose-dependent effect on supine diastolic blood pressure. Such differences in safety and tolerability may be important in particular patient populations. There also appears to be a substantial difference between venlafaxine and the SSRIs with respect to their tolerability in overdose; in fact, venlafaxine appears to have similar mortality in overdose to the TCAs. Tolerability should therefore be considered when classifying newer antidepressants as first- or second-line medications. In summary, current data do not provide robust evidence for greater efficacy of multi-action agents over selective compounds such as SSRIs, although there is evidence suggesting safety and tolerability differences. Clinical data should be evaluated carefully before conclusions are accepted, and treatment outcomes, including safety and tolerability, should remain the focus when treating patients with depression and anxiety disorders.

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LS-02-04

Treating anxiety disorders: Efficacy and safety considerations

B. Bandelow. *University of Göttingen Dept. of Psychiatry, Göttingen, Germany*

Anxiety disorders are highly prevalent, representing the most common group of psychiatric illnesses. These conditions can be disabling to the patient and costly to healthcare systems. Despite their prevalence, anxiety disorders often go undiagnosed and untreated. Diagnosis may be complicated by the typical presentation of multiple, unexplained somatic complaints and comorbid disorders. Selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs) are now generally considered first-line therapies for a variety of anxiety disorders. However, recent data indicates that there are potential safety problems with certain SNRIs, which should be considered when selecting appropriate, safe medications, and when defining first- and second-line treatments. The safety and efficacy of SSRIs and SNRIs in children is also currently under discussion. This session will review data supporting antidepressant efficacy in conditions including panic disorder, obsessive-compulsive disorder, social anxiety disorder, generalized anxiety disorder, and post-traumatic stress disorder. When selecting a suitable treatment for patients with anxiety disorders, the safety and tolerability profile of an agent should be considered in addition to efficacy. The SSRIs are

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structurally diverse and have differing pharmacodynamic and pharmacokinetic profiles, which are likely to impact upon the clinical management of this patient population (eg, drug-drug interactions, discontinuation syndrome). Safety and tolerability data from a number of SSRIs will be evaluated with respect to adverse events and undesirable effects on cognition. Some SSRIs are associated with significant changes in weight during long-term treatment, and cessation of certain antidepressants has been associated with discontinuation syndrome. The potential of SSRIs to cause drug-drug interactions is also an important consideration when selecting treatment, particularly since patients with mood and anxiety disorders have high rates of medical and psychiatric comorbidity and are likely to be taking concomitant medications.

Chair's closing remarks

D. Sheehan. *University of South Florida College of Medicine, Tampa, USA*

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