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Early onset of antipsychotic action and outcome of Ziprasidone treatment in placebo-controlled bipolar mania trials

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Background and Aims: Recent research indicates intramuscular ziprasidone produces a significant, early (within 24 hours) improvement in psychotic symptoms. In this analysis, we evaluated the potential for an early antipsychotic response to oral ziprasidone in subjects with acute bipolar mania.

Methods: We conducted a pooled analysis of two 3-week, randomized, double-blind, placebo-controlled trials of ziprasidone (40-160 mg/d) in hospitalized patients (N=415) with bipolar I disorder, and a current manic (N=257) or mixed episode (N=158), with (N=151) or without (N=245) psychotic features. Efficacy assessments included the Mania Rating Scale (MRS, derived from the SADS-C). Remission was defined as achieving a MRS score \leq 12. Improvement in psychosis was evaluated by a sum of the three SADS-C psychosis items (delusions, hallucinations, and suspiciousness). MMRM and logistic regression analyses were applied to estimate the time course of response.

Results: Significantly greater response rate (>50% decrease from baseline) and improvement in the SADS-C psychosis score were observed in the ziprasidone group (versus placebo) as early as Day 4 ($p < 0.01$), and the magnitude of improvement increased with time ($p < 0.003$). At Day 21, remission rate with ziprasidone monotherapy was 49% versus 36% in the placebo group ($p = 0.02$). Early antipsychotic response at Day 4 was an accurate predictor of remission at Day 21 ($p < 0.01$, ROC=0.76).

Conclusions: Ziprasidone was associated with a rapid onset of response in psychotic symptoms in patients with acute bipolar mania. This early reduction in psychotic symptoms was found to mediate overall improvement in manic symptoms and predict remission at endpoint.

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The prevalence of mixed episodes during the course of illness in bipolar disorder

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Aim: To investigate the prevalence of mixed episodes during the course of illness in bipolar disorder.

Methods: A total of 1620 patients with an ICD-10 diagnosis of bipolar affective disorder at the first psychiatric contact were identified in a period from 1994 to 2003 in Denmark and the prevalence of mixed, depressive and hypomanic/manic episodes were calculated at each episode.

Results: The prevalence of mixed episodes increased from the first episode to the tenth episode, however, only for women (6.7 % of the first episodes leading to psychiatric care compared to 18.2 % of the tenth episodes). For men, the prevalence of mixed episodes was constantly low. At all episodes, the presence of a current mixed episode increased the risk substantially of getting a future mixed episode.

Conclusion: Clinicians should pay more attention to mixed episodes, especially among women, as they may represent an increasing treatment challenge as the illness progress.

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Outcomes of acute mania: 12 month results from the french EMBLEM cohort

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Objectives: To describe 12 month outcomes of French patients enrolled in EMBLEM (European Mania in Bipolar Longitudinal Evaluation of Medication).

Methods: EMBLEM is a prospective, observational study on outcomes of manic/mixed episode. Adult patients were enrolled within the standard course of care if they initiated/changed oral medication for treatment of acute mania. All treatment decisions were at the discretion of the treating psychiatrist. 530 psychiatrists (126 French) enrolled 3459 eligible patients (771 French). 12 months results of the French cohort will be presented.

Results: At baseline, mean age was 45.5 years (sd 13.6) and 59% were female. 68% were outpatients and 34% had a mixed episode. 76% of French patients were eligible for follow-up at 12 months. 80% improved (CGI-BP overall decrease > 2) during follow-up whereas 47% patients never achieved recovery (two consecutive CGI-BP overall < 2). 37% of patients presented with no medication at baseline. 41.6% were started on monotherapy and 58.4% on combination therapy; of those 54% and 28% respectively remained on their initial medication throughout the 12 months. 25% were treated with antidepressants in addition to their new oral medication, which increased to 35% at 12 months.

Conclusions: In this naturalistic study, less than half of French patients achieved recovery during 12 months follow-up. Antidepressant was frequent at baseline and use increased during follow-up. Twice as many patients remained on the same monotherapy as those on the same combination therapy

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Low serum total cholesterol in bipolar disorder

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Background and Aims: Low serum total cholesterol has been reported to be associated with risk of suicidal, violent and impulsive behaviours. To date there are no laboratory tests for diagnosing bipolar disorder (BD). Case vignette to illustrate the clinical observation of changes of serum total cholesterol (STChol) and mood disturbances of patient with bipolar disorder (BD) at admission and in remission was used.

Methods: A 23- years old, healthy and drug-free female met the ICD-10 criteria for bipolar disorder. She was assessed during two mixed episodes to explore change in serum cholesterol (Chol) levels at admission (A) of first (1e) episode and after remission (R), one month later. The readmission due to second consecutive mixed episode (2e) was 19 months later. MADRS scale for depression and YMRS scale for mania were applied, and body mass index (BMI) was assessed.

Results: Chol-1eA 2,50 mmol/l (normal range 3,63-6,20 mmol/l), Chol-1eR 3,90 mmol/l; Chol- 2eA 3,05 mmol/l. BMI-1e 20,5 BMI-2e

21.0. YMRS-1eA score 27, YMRS-1eR score 4, MADRS-1eA score 23, MADRS-1eR score 3, YMRS-2eA score 23, MADRS-2eA score 21. The patient did not change her diet during the course of illness.

Conclusions: In this case low STChol was associated with the onset of mixed episodes of BD and normalised after remission of episode. Low STChol could be a state marker or risk factor for mixed episode of BD. Further investigations are needed to explore the possible relationship between STChol and course of different episodes of BD.

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Familial loading in bipolar disorder and substance use disorder

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Background: Bipolar disorder and substance use disorder have well documented genetic component. Among Axis I disorder bipolar subjects have highest comorbidity for alcohol and substance use disorder, ranging from 17 to 60%. Some Authors find a familial association between bipolar disorder and substance use disorder, suggesting the question if these disorders share a common genetic liability.

Aims: To investigate familial loading in bipolar disorder (with and without alcohol/substance use disorder) and in patients with substance use disorder.

Methods: Sampe (62 patients with bipolar disorder and alcohol/substance use disorder-DD, 23 patients with bipolar disorder-BD, 22 patients with substance use disorder without mood disorder-SUD) was recruited in Psychiatric clinic of Pisa and Dependence Department of Pisa and Bolzano. Instruments: SCID-IV-I/P for Axis I diagnosis and Family History Screen (Weissman, 2000).

Results: Bipolar pts (DD and BD) have higher familial diathesis for manic and depressive episodes respect DUS probands ($p \leq 0.001$). Moreover DD show higher familial loading for alcohol/substance use respect BD ($p=0.000$). Abuser subjects (DD and SUD) show higher familiarity for conduct disorder respect BD ($p=0.008$)

Conclusions: DD pts show a double familial loading, both for mood disorder (respect SUD), and for alcohol/substance use disorder (respect BD). Probably the familial loading for substance use disorder and mood disorder are distinct and they are both present in dual diagnosis patients.

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Comorbidity between personality disorders and bipolar disorders

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Introduction: The complex interrelationship between personality disorders and bipolar disorders is still a controversial aspect with multiple diagnosis, therapeutic and etiologic implications.

Comorbidity has been defined as the presence of more than one disorder in the same patient at the same time.

Methods: We made a literature review between 1995 and 2005 about comorbidity in bipolar and personality disorders.

Results: There are different studies that agree the theory that personality disorders are previous forms of bipolar disorders.

Besides, it is important to consider the effect that bipolar disorders have over personality.

In the last years, different authors have suggested that co-morbid personality disorders predict a worse evolution in the course of the bipolar disorders, finding recurrent and resistant to treatment affective symptoms.

The co-occurrence studies of personality and affective disorders have ranged from 3 to 70%.

If we take the global n (428) of all the reviewed articles, we see that the percentage of comorbidity between personality disorders and bipolar disorders is almost the 48% of the studied patients. Looking at the most prevalent cluster, cluster A is the 13%, cluster B is near the 39% and cluster C the 35%.

Conclusion: Personality traits, dimensions and personality disorders seem to play an important role in the evolution of bipolar disorders.

The identification of these specific personality traits and the knowledge of the influence in the evolution of the illness are extremely important in the treatment and prevention of bipolar disorders.

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Bipolar depression. Characteristics in a first episode of bipolar sample

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Background and Aims: Depression is highly recurrent in Bipolar patients, causes more disability than other manifestations of the illness and depressive symptoms predominate over manic and hypomanic symptoms. Our aim is to describe whether in our sample we can find some specific differences from the early course of the illness.

Methods: 33 patients meeting DSM-IV criteria of Bipolar Disorder I and II whose illness onset was less than 5 years from the first Manic/ hypomanic episode or/and less than 10 years from the index depressive episode. Recorded variables included socio-demographic, clinical, treatment characteristics and scales (HRSD, YMRS, BPRS, GAF). Analysis was performed using SPSS Version 12.0.

Results: 57.6% were male, 42.4% female, mean age 34.42 years. 2 Patients (6.2%) were depressed when inclusion and 8.8% had had a depressive episode before were included in our Program.

The mean number of depressive episodes was 1.88 (SD 3.58). Only 1 patient had had self-harm intent. 15.2% has first degree family history of Unipolar depressive disorder and 20% of Bipolar disorder. 6.2% were hospitalized because a depressive episode.

Conclusions: We found less rates of depressive episodes than we found in the literature with less sub-syndromal and syndromal depressive symptoms than in routine bipolar population that could be explained by the short course of the illness in our sample. More research should be done to study bipolar depression in early phases to find predictors that help us to decrease the high impact it has in the disorder.

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Development and evaluation of a new patient-reported instrument: The Bipolar functional status questionnaire

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