FC58-4

RECOVERY IN AFFECTIVE DISORDER — A CASE REGISTER STUDY

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Background: It is unclear how the duration of episodes changes during the course of unipolar and bipolar affective disorder.

Method: The rate of recovery was estimated with survival analyses at successive episodes in a case register study including all hospital admissions with primary affective disorder in Denmark during 1971–1993.

Results: A total of 9,174 patients with recurrent episodes were followed from their first admission. The rate of recovery did not change with the number of episodes in unipolar or in bipolar disorder. This result is in accordance with findings from recent decades whereas the majority of studies from the era before the introduction of effective treatment have found an increasing duration of episodes during the course of illness.

Conclusion: The duration of episodes in untreated unipolar and bipolar affective disorder seems to increase as the illnesses progress whereas in modern treatment settings it is possible to stop this deteriorating course.

FC58-5

MORTALITY IN ADOLESCENTS ADMITTED WITH A DIAGNOSIS OF AFFECTIVE DISORDER (DEPRESSION AND BIPOLAR DISORDER)

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Objective: To study the mortality in a large, nation-wide cohort of adolescents admitted with depression.

Methods: Using the Nation-wide Danish Psychiatic Case- Register, the study analyzes all adolescents, aged 13–19 years, who had been admitted to a psychiatic department during the years 1970–93. Combining with information from the nation-wide Death register, the prognosis, as regards mortality, was described.

Results: Compared to an age- and sex-standardized group form the normal population, the cohort had a considerable increased mortality. The SMR (standardized mortality ratio) was 5.54 for males (CI 3.71–7.96), and 8.76 for females (CI 5.76–12.93). The SMR for suicide was 19.85 for males (CI 12.44–30.05) and 37.77 for females (CI 23.07–58.33). The distribution of death causes and the time from admissions to death will be presented.

Conclusions: Adolescents diagnosed with affective disorders are at great risk for premature death. The treatment implications will be discussed.

FC58-6

TREATMENT OF ACUTE MANIC EPISODES WITH VALPROATE AS AN ADJUNCT TO NEUROLEPTIC MEDICATION

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In a multicentre randomised double-blind trial 136 patients hospitalised for acute manic episodes (ICD 10) received either 20 mg/kg sodium valproate (Orfiril®) or placebo in addition to basic treatment with neuroleptics for 21 days. Investigators were required to reduce the dosage of the individual neuroleptic on day 5, 10 and 15 by one third of the last dose administered or according to the clinical condition. Psychopathological ratings by means of the Young Mania Rating Scale, Global Assessment Scale (GAS) and Clinical Global Impression (CGI) were performed at various time points. The safety was evaluated on the basis of the occurrence of adverse events. The total dosage of neuroleptics expressed as haloperidol-equivalents was the primary target parameter.

The neuroleptic dose (haloperidol-equivalents) declined continuously in the valproate group from 14.3 ± 9.4 mg on the first study day to 8.2 ± 6.9 mg on the last day, while values varied in the placebo group between 12.0 ± 6.6 mg and 10.4 ± 9.6 mg. A statistically significant difference in the daily neuroleptic dose was found for the second and third study weeks ($p = 0.0007$, two-tailed). The severity of manic symptoms decreased in the course of the study from 30.9 ± 8.1 to 11.6 ± 9.3 and from 30.9 ± 8.4 to 17.9 ± 10.9 in the valproate and placebo group, respectively ($p = 0.0042$). Mean GAS scores increased from 40.4 ± 10.3 to 63.8 ± 16.3 in the valproate group and from 41.0 ± 10.8 to 56.7 ± 18.7 in the placebo group ($p = 0.0108$).

18 patients dropped out prematurely, 7 of the valproate group and 11 of the placebo group. No serious adverse events occurred. The combination of valproate and neuroleptics was well tolerated and did not lead to increased occurrence of adverse events. In conclusion, the study clearly demonstrates the clinical effectiveness and safety of valproate as an adjunct to neuroleptic medication in patients with acute manic episodes.

FC58-7

A COMPARISON OF SYMPTOMS FOLLOWING TREATMENT INTERRUPTION: EVIDENCE FROM A RANDOMIZED, DOUBLE-BLIND TRIAL WITH FLUOXETINE, SERTRALINE, AND PAROXETINE

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Introduction: Evidence suggests that shorter acting SSRIs compared with fluoxetine are often associated with increased adverse events and dysphoria during brief treatment interruptions. Previous studies are limited by lack of prospective patient randomization; only one was conducted under controlled conditions. We report a prospective, randomized, double-blind study assessing effects of SSRI interruption following successful initial treatment of depression.

Methods: Drug-free outpatients (N = 284) with major depression were randomized under double-blind conditions to fluoxetine, sertraline, or paroxetine treatment. Responders following 4–10 weeks of acute treatment (N = 213; fluoxetine = 67, sertraline = 75, paroxetine = 71) went into a 5-month continuation phase. Treatment was then interrupted for 4–6 day periods under double-blind conditions. Adverse event (AEs) were solicited by systematic inquiry.

Results: Before treatment interruption, all groups had similar AEs and HAMD scores. Following interruption, new or worsened AEs were more frequent among paroxetine-treated than fluoxetine-treated or sertraline-treated patients ($p < .001$, $p = .006$; respectively) and showed a trend for greater frequency among sertraline-treated patients compared with fluoxetine-treated patients ($p = .086$). Paroxetine-treated patients showed a trend for return of depressive symptoms compared with fluoxetine-treated patients ($p = .074$).

Conclusion: These results provide evidence from a prospective, randomized, double-blind study that brief interruption of SSRI