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Research report

Do young adults with bipolar disorder benefit from early intervention? ☆

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ABSTRACT

Background: It is unknown whether young adults with bipolar disorder are able to benefit from early intervention combining optimised pharmacological treatment and group psychoeducation. The aim of the present report was to compare the effects of early intervention among patients with bipolar disorder aged 18–25 years to that of patients aged 26 years or older.
Methods: Patients were randomised to early treatment in a specialised outpatient mood disorder clinic versus standard care. The primary outcome was risk of psychiatric re-hospitalisation.
Results: A total of 158 patients with mania/bipolar disorder were included among whom 29 (18.4%) were between 18 and 25 years and 129 patients were 26 years or older. For both age groups, the point estimate of the hazard ratio of re-hospitalisation was insignificantly decreased for patients treated in the mood disorder clinic versus standard treatment but more so for patients between 18 and 25 years (HR 0.33, 95% CI 0.10–1.07; $p=0.064$) than for patients 26 years or older (HR 0.68, 95% CI 0.40–1.14, $p=0.14$). Younger adults treated in the mood disorder clinic used mood stabilisers and antipsychotics more in contrast to those treated in standard care. The differences between the estimates of effects did not reach significance in tests of interactions ($p>0.2$).
Limitations: The study was based on a post hoc subgroup analysis and due to the small number of patients aged 18–25 years, type II errors cannot be excluded.
Conclusions: Although not statistically different, the observed differences of the point estimates was surprisingly larger for young adults suggesting that young adults with bipolar disorder may benefit even more than older adults from early intervention combining pharmacological treatment and group psychoeducation.

1. Introduction

Bipolar disorder may on average have a progressive course of illness with poor long-term outcomes. The risk of relapse of episodes is high and increases with the number of previous episodes (Kessing et al., 2004a, 2004b). A large proportion of patients do not recover to previous psychosocial function (Tohen et al., 2000; Conus et al., 2006) and develop sustainable cognitive impairment (Torres et al., 2007) and even dementia in the long run (Kessing and Nilsson, 2003). Early combined pharmacological and psychological intervention in bipolar disorder has recently attracted much interest and has been suggested to improve long-term outcomes (Berk et al., 2007, 2009; Macneil et al., 2011, 2012a, 2012b) but only one randomised clinical trial has specifically investigated the effects of such interventions in the early stages of bipolar disorder (Kessing et al., 2013). In that randomized clinical trial, we recently showed that early intervention in a specialised mood disorder clinic combining optimised pharmacological treatment and group psychoeducation significantly reduced psychiatric re-hospitalisation, increased use of mood stabilisers and antipsychotics, and increased patient satisfaction compared with treatment in standard care (Kessing et al., 2013).

☆ **Trial registration** ClinicalTrials.gov: ID: NCT00253071.

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Early onset bipolar disorder has been associated with greater severity, high level of comorbidity including substance abuse, resistance to mood-stabilisers and poorer long-term outcome including disturbed interpersonal relationships, academic failure, high rates of suicide attempts and completions, and multiple hospitalisations (see review by Leboyer et al. (Leboyer et al., 2005)). Consequently, it has been discussed whether young adolescents and adults are able to benefit from early intervention (Berk et al., 2007) facing challenges such as interference of illness with age-specific educational, social and psychological development (Berk et al., 2007) as well as poor insight (Robinson et al., 2009), poor adherence to treatment (Gonzalez-Pinto et al., 2010; Bates et al., 2010) and higher comorbidity with alcohol and other substance use (Conus et al., 2006) compared to older adults (Berk et al., 2007). It has, however, never been investigated in any trial whether younger patients benefit less or more from early intervention compared to older adults. Patients included in our early intervention trial (Kessing et al., 2013) had a rather high age at inclusion in the trial with a median age of 35.6 years, but 18.4% of the patients were between 18 and 25 years of age. Overall, age of the patients was in accordance with findings in observational studies recruiting patients following first hospitalisation (mean age 31.4+12.9 and 38.4+12.6 years, respectively (Khalsa et al., 2008; Perugi et al., 2000)). The clinical impression was that younger patients benefitted from the treatment programme in the mood disorder clinic.

The aim of the present report was to compare the effects of early intervention combining optimised pharmacological treatment and group psychoeducation among patients with bipolar disorder aged 18–25 years to that of patients aged 26 years or older. It should be emphasised that the original trial was not designed to test whether age at inclusion interact with the intervention effect, so this study represents a post hoc subgroup analysis. The trial design was pragmatic with very few exclusion criteria and investigated the effect among patients following psychiatric hospitalisation in The Capital Region of Denmark for the first, second or third time with a diagnosis of mania or bipolar disorder. This pragmatic design was chosen to obtain a high generalisability of the results from the trial to clinical settings regarding patients early in the course of bipolar disorders (Zwarenstein et al., 2008).

2. Methods

The trial protocol has been described in detail elsewhere (Kessing et al., 2013, 2011). In short, the trial included a total of 158 patients who were discharged from their first, second, or third hospitalisation from an inpatient psychiatric ward with an ICD-10 diagnosis of single manic episode or bipolar disorder (ICD-10 code: F 30.1–31.6) as the primary diagnosis. Patients were recruited from seven psychiatric wards in The Capital Region of Denmark during a period from December 2005 to December 2009. The vast majority suffered from a bipolar I disorder. Comorbidity with alcohol or substance abuse and other psychiatric disorders were allowed. The only exclusion criteria were moderate or severe dementia, poor understanding of Danish, or any kind of commitment. Patients were randomised 1:1 to the intervention group or the control group at the end of the index hospitalisation while still in hospital. The Copenhagen Trial Unit conducted randomisation centrally according to a computer generated allocation sequence to secure allocation concealment. Allocation was stratified for psychiatric centre and number of previous hospitalisations before the index hospitalisation (0 or >1). The randomisation was carried out with a block size of 20 unknown to the investigators. The primary outcome measure was psychiatric re-admission based on public register data (Mors et al., 2011) using blinding for intervention. All other outcomes were based on a questionnaire mailed to patients 1 and 2 years after randomisation and were assessed without blinding to the intervention. The questionnaire included formalised questions on mood symptoms, satisfaction with care and the use of mood stabilisers (lithium or anticonvulsants), atypical antipsychotics, and/or antidepressants. For each variable, data on questionnaires were combined for the 1 and the 2 years responses into one combined measure.

Patients in the experimental intervention group were treated in a specialised outpatient mood disorder clinic, The Copenhagen Affective disorder Clinic, the Capital Region of Denmark at the Psychiatric Centre Copenhagen, Copenhagen University Hospital, Rigshospitalet. The staff in the outpatient mood disorder clinic consists of full time specialists in psychiatry with specific clinical experience and knowledge on diagnosis and treatment of bipolar disorders as well as certified psychologists, nurses, and a social worker with experience in bipolar disorders. The clinic offers combined intervention with evidence based pharmacological treatment and group psychoeducation. Manuals for psychoeducation were developed, tested, and revised in a pilot phase with inclusion of approximately 30 patients. The intervention programme lasted 2 years. According to the protocol, a medical doctor evaluated all patients in the clinic as early as possible following discharge from inpatient hospitalisation and no later than 2 weeks after discharge as this is a vulnerable period. Prior course of illness and effect of treatment was carefully recorded and diagnosis and treatment plans were re-evaluated and current pharmacological treatment adjusted in accordance with clinical status and with an approach very similar to the revised recommendations from the British Association for Psychopharmacology that was published in 2009 (Goodwin, 2009). Thus, focus was on treatment with mood stabilisers, mainly lithium, valproate, lamotrigine, and atypical antipsychotics (for further details see Kessing et al. (2013)). Antidepressants were only employed when remission could not be obtained in other ways and in that case mainly SSRI's combined with one or two mood stabilisers (Goodwin, 2009).

The psychological intervention has been described in details elsewhere (Kessing et al., 2013, 2011). Patients participated in three different sequential group sessions. The first group was a settling-in group for patients just discharged from hospitalisation with the aim of obtaining at least partly remission (scores on Hamilton Depression Rating Scale-17 items <14 and on Young Mania Rating Scale <14), i.e., typically for some months up to half a year. When stable, the patients were transferred to the second group, a psychoeducation group for 1½ h intervention every week for 12 consecutive weeks followed by three additional booster sessions. In the psychoeducation group focus was on knowledge and acceptance of suffering from a bipolar disorder, identifying depressive and manic symptoms from normal reactions, personal identity in relation to suffering from a bipolar disorder, risk situations, stress management, the need for sustained pharmacological maintenance treatment, adverse effects to treatment, and identification of individual early warning signs of upcoming depressive and manic episodes. In addition, in some sessions cognitive behavioural therapeutic approaches were included focusing on cognitive distortions in identity and behaviour and to some extent on inter-individual conflicts. Finally, patients joined a 3–6 months discharge group that was a preparation for re-referral either to the general practitioner, a private psychiatrist, or to the community psychiatric centre. Six to eight patients and two therapists (psychiatrist and psychologist or nurse) participated in each group.

The control group was offered standard care consisting of the standard outpatient mental health service routines in The Capital Region of Denmark, i.e., treatment at the general practitioner,