Journal of Affective Disorders 150 (2013) 1055–1061

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Acute and long-term treatment outcome in depressed inpatients with vs. without anxious features: Results of a one-year follow-up study ☆

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ARTICLE INFO

Article history:
Received 22 April 2013
Accepted 17 May 2013
Available online 10 June 2013

Keywords:
Depression
Anxiety
Anxious depression
Treatment outcome
Acute treatment
Follow-up

ABSTRACT

Background: Anxious depression (AD) is common in patients with unipolar depression. It remains unclear if they have a higher level of depressive symptoms, a higher risk of non-response, a poorer prognosis and a higher relapse rate compared to non-anxious depressed (non-AD) patients.
Methods: 168 patients took part in all three measurement points: (1) intake, (2) discharge and (3) follow-up. Patients fulfilled the criteria for anxious depression if they had a baseline score >7 on the anxiety/somatisation factor of the Hamilton Rating Scale for Depression (HRSD). Patients with AD and non-AD were compared regarding symptom reduction from intake to discharge as well as from discharge to one year after discharge. Primary outcome measure was the HRSD.
Results: The prevalence of AD was considerably high (81%). At intake, patients with AD had a significant higher score in the modified HRSD ($M=20.67\pm4.12$ vs. $M=14.35\pm5.06$). Both patient groups showed a significant and comparable intake-to-discharge symptom reduction in all inventories. Remission rates at discharge did not differ between AD and non-AD patients. At 1-year follow-up, AD patients showed a similar symptom severity compared to non-AD patients.
Conclusion: Symptoms of anxiety are common in depressive disorders are associated with higher depressive symptoms at the beginning of treatment. Acute and longer-term treatment outcome of AD patients was comparable to that of non-AD patients.
Limitations: Limitations of this study are the naturalistic design, treatment was not standardized and comorbid anxiety disorders were not assed using a structured interview.

1. Background

Major depressive disorder (MDD) – with a lifetime prevalence of 15% – is one of the most frequent mental disorders. It causes loss of life-quality, disability and is even related to early death. According to Kessler et al. (2003) as well as Lopez et al. (2006) depression will be at third place of costs for the health care system in 2020. Although, several pharmacological treatment options for MDD exist, different studies show only modest remission rates. For example, in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial (Rush et al., 2006), the remission rate for depressed outpatients who initially received monotherapy with citalopram was only 33%. Nevertheless, remission of symptoms should be the aim of treatment because patients whose depression has remitted after treatment have a higher overall functioning and a better prognosis than patients without symptom remission (Trivedi and Daly, 2008).

Comorbid mental disorders can affect the clinical presentation, course of illness, and treatment outcome of MDD. Especially, anxiety and substance abuse disorders are commonly present in patients with MDD (Davis et al., 2006; Kessler et al., 2003; Rush et al., 2005). Although depression and anxiety are considered to be distinct disorders, the majority of depressed patients also suffer from anxiety-related symptoms, independent of the presence of a comorbid anxiety disorder (Fava et al., 2008). Some authors argue that anxious depression is a subtype of MDD that researchers as well as therapists should draw special attention on, e.g. regarding

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http://dx.doi.org/10.1016/j.jad.2013.05.043

pharmacological treatment [8]. Nevertheless, the current classification systems do not distinguish between non-anxious depression and anxious depression, as a subtype of MDD (Levine et al., 2001). To answer the question whether the distinction between non-anxious and anxious depression is meaningful it is important to assess the clinical relevance of the concept of anxious depression. One way to do this is to evaluate its external validity by examining the impact of anxious depression on the treatment outcome in depression.

With respect to the existing evidence, there is still uncertainty whether depressed patients with features of anxiety have higher levels of depressive symptoms pre- and post-treatment as well as a higher risk of non-response and chronicity than depressed patients without profound anxiety symptoms. In STAR*D (Rush et al., 2006) the subgroup of patients with anxious depression, defined by a score ≥7 on the anxiety/somatisation factor of the Hamilton Depression Rating Scale (Cleary and Guy, 1977), were less likely to respond, had a longer time to remission and were more intolerant to pharmacological treatment (side effect frequency, intensity and burden) than depressed patients without anxious depression (Fava et al., 2008). Furthermore, patients with features of anxious depression were different to depressed patients without anxious symptoms regarding sociodemographic characteristics such as gender, age, educational and family status (Fava et al., 2006). They were more likely to have a later onset of depression, a lower school education and more often lived alone. Consistent with the study from Fava et al., in a study of the German Algorithm Project (Wiethoff et al., 2010) a subgroup-analysis of patients with anxious depression revealed a poorer treatment outcome compared to patients without anxious depression. In that study the prevalence of anxious depression, also defined by the anxiety/somatisation factor of the Hamilton Depression Rating Scale, was 49% and remission was less likely to be achieved and took longer to occur in anxious depressed patients, compared to non-anxious depressives. In both studies there was no specific additional psychotherapeutic treatment. Nevertheless, one has to keep in mind that all studies comparing anxious and non-anxious depression were uncontrolled studies. Therefore, it is questionable if the "specific effects of antidepressants were reduced or if overall response rates were lower because anxious patients were less responsive to the nonpharmacologic elements of treatment" (Nelson, 2010). To answer this question, Nelson (2010) conducted a meta-analysis including results from 11 studies. The results of this meta-analysis indicate that the drug-placebo treatment difference was unaffected by anxious status. Nevertheless, in a further meta-analysis by Davidson et al. (2002) it could be shown that remission rates were reduced in depressed patients with high anxiety features as assessed at end of treatment.

However, several questions remain unaddressed: (1) Is the lower remission rate in anxious patients related to their higher pre-treatment depression level? and (2) Does the prevalence of anxious features predict a poorer prognosis and a higher relapsing rate in the course of symptomatology in a follow-up period? The aim of this study is to make a contribution to the answer of these clinical relevant questions and – by doing so – to add evidence to the external validity of the concept of anxious depression.

2. Methods

2.1. Participants

Patients were recruited from the psychiatric unit of the 'Theodor-Wenzel-Werk' clinics in Berlin, Germany. Patients were included if they had (1) a major depressive episode or recurrent depression as the principal current diagnosis according to ICD-10, (2) an age ≥18 years and (3) a score ≥15 on the 17-item version of the Hamilton Rating Scale for Depression and/or a score ≥18 on the Beck Depression Inventory at admission, indicating a clinical relevant severity of depression in an expert-and/or a self-rating scale (Frank et al., 1991). The study has been conducted in accordance with the current version of the Declaration of Helsinki and was approved by the local Ethics Committee. Participants were excluded from the study if they had (1) a previous history of schizophrenia, schizoaffective disorder or bipolar I disorder, (2) an acute withdrawal syndrome induced by the use of psychoactive substances or (3) language as well as concentration- and thinking deficits to an extent that they could not complete the questionnaires. Furthermore, patients were excluded from the study if the depressive episode was attributable to organic illness.

2.2. Treatment

Treatment was multidisciplinary. All patients were treated with psychopharmacological medication and clinical management. If indicated according to the German national clinical practice guideline for unipolar depression (Härter et al., 2010), patients took part in occupational therapy (91%), sports therapy (85%), cognitive-behavioural group therapy for depression (68%), individual cognitive-behavioural therapy (53%), motion therapy (40%), music therapy (24%), cognitive-behavioural group therapy for anxiety disorders (20%), progressive muscle relaxation training (19%), addiction therapy (8%), art therapy (4%) and light therapy (2%). The inpatient treatment lasted an average of 59.2 ± 29.2 days.

In the first year follow-up, 71% of the patients had an outpatient psychiatric treatment, 65% took part in individual psychotherapy, 18% were treated in a psychiatric day clinic and 24% had a psychiatric inpatient retreatment.

2.3. Assessment

2.3.1. Social, demographic and clinical variables

The diagnosis of a major depressive episode or a recurrent depression was given by the attending psychiatrist using the International Diagnostic Checklist for ICD-10 and DSM-IV for Depressive Episodes (IDCL (Hiller et al., 2005)). To measure depression severity the 17-item version of the Hamilton Rating Scale for Depression (HRSD (Hamilton, 1960)) and the Beck Depression Inventory (BDI (Beck et al., 1961)) were used. Additionally, the Global Assessment of Functioning Scale (GAF (Endicott et al., 1976)) and the Clinical Global Impression Scale (CGI (Guy, 1976)) were used. The HRSD was administered by an experienced clinical psychologist. The GAF and CGI were administered by the attending psychiatrist who received training in the use of the IDCL, GAF and CGI. Furthermore, the global symptom distress was assessed by the Global Severity Index of the Brief Symptom Inventory (BSI–GSI (Derogatis and Melisaratos, 1983)). All symptom ratings were performed within four days after admission and four days before discharge. Information about comorbid axis I disorders and treatments obtained were gained by chart review post-treatment.

2.3.2. Follow-up

Approximately one year ($M = 15.5 \pm 1.5$ months) after discharge, patients were contacted again. The evaluation included BDI, BSI and a questionnaire to collect information about treatment during the first year after inpatient treatment. The HRSD was administered via telephone by a trained clinical psychologist.