European Psychiatry 28 (2013) 288–292

Available online at
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Original article

Fast versus slow onset of depressive episodes: A clinical criterion for subtyping patients with major depression

U. Hegerl [a,*], R. Mergl [a], D. Quail [b], E. Schneider [c], M. Strauß [a], H.-P. Hundemer [c], M. Linden [d]

[a] Department of Psychiatry, University of Leipzig, Semmelweisstr. 10, 04103 Leipzig, Germany
[b] Lilly UK, Department European Medical Information Sciences, Windlesham, Surrey GU20 6PH, United Kingdom
[c] Lilly Germany, Medical Department, Division of Neuroscience, Werner-Reimers-Str. 2-4, 61352 Bad Homburg, Germany
[d] Research Group Psychosomatic Rehabilitation at the Charité, University Medicine Berlin and the Rehabilitation Centre Seehof, Lichterfelder Allee 55, 14513 Teltow/Berlin, Germany

ARTICLE INFO

Article history:
Received 4 November 2010
Received in revised form 31 January 2012
Accepted 14 February 2012
Available online 26 April 2012

Keywords:
Depression
Mood disorders
Speed of onset
Multi-centre trial

ABSTRACT

Purpose. – The speed of onset of depressive episodes is a clinical aspect of affective disorders that has not been sufficiently investigated. Thus, we aimed to explore whether patients with fast onset of the full-blown depressive symptomatology ($\leq$ 7 days) differ from those with slow onset ($>$ 7 days) with regard to demographic and clinical aspects.
Subjects and methods. – Data were obtained within an observational study conducted in outpatients with major depression who were treated with duloxetine (30–120 mg/day). Onset of depression (without any preceding critical life event) was fast in 416 (less than one week) and slower in 2220 patients.
Results. – Compared to patients with slow onset, those with fast onset of depression had more suicide attempts in the previous 12 months (2.7% versus 1.3%, $P = 0.046$) and less somatic comorbidity (61.7% versus 74.1%, $P < 0.0001$). In addition, they were slightly younger at onset of depression (mean $\pm$ SD 40.2 $\pm$ 14.6 versus 42.8 $\pm$ 14.2 years, $P < 0.001$) and used analgesics at baseline significantly less frequently (22.8% versus 33.4%, $P < 0.0001$).
Discussion and conclusion. – The speed of onset of depression has to be regarded as a relevant clinical characteristic in patients with unipolar depression.

1. Introduction

It is well known to clinicians that patients with depressive disorders differ considerably in the speed of onset of depressive episodes. Many patients develop the full-blown depressive symptomatology slowly over weeks and months. Others show an abrupt onset within hours even without an external trigger. Clinical experience and empirical data suggest that the time course of onset is similar in different episodes and a disease-associated trait in patients with recurrent depression [8]. Surprisingly, systematic studies of this clinical aspect are largely absent. An important exception is the study by Sauer et al. [12] who tested the value of clinical and neuroendocrinological variables for the prediction of the amitriptyline response in patients suffering from DSM-III major depressive episodes. In this context, "DSM-III depressive psychotic features, DSM-III personality disorder and sudden onset of illness were significantly associated with poor treatment response and explained 34% of the outcome variance" ([12], p. 284). Using a newly developed onset of depression inventory (ODI), we recently found a clearly faster onset in patients with bipolar versus unipolar depression [8] (also [6]). In 58% of patients with bipolar depression, the symptomatology developed within 1 week, whereas this was the case in only 7.4% of patients with unipolar depression [6]. This finding raises the question as to whether, within unipolar depression, patients with fast versus slow onset of depression also differ in respect of clinical and pathophysiological aspects. Such differences are probable since depression with slow onset might coincide with chronic depression and chronic depression may be associated with characteristic features like protracted environmental stress and increased stress reactivity [10].

The aim of the study was to investigate the associations between speed of onset and clinical aspects (time to mood response) and demographic aspects in a large group of patients with unipolar depression within an exploratory approach.

2. Subjects and methods

2.1. Patients and recruitment

Data were gathered within an observational study [13] (Painful Physical Symptoms in Depressed Patients: Relation to Treatment

* Corresponding author. Tel.: +49 341 9724 530; fax: +49 341 9724 539.
E-mail address: Ulrich.Hegerl@medizin.uni-leipzig.de (U. Hegerl).

0924-9338/$ – see front matter © 2012 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.eurpsy.2012.02.002

Outcomes in Clinical Practice) (PADRE), a prospective multi-centre non-interventional study with a duration of 6 months.

The study was performed at 693 centers in Germany. To minimize the selection bias, all psychiatrists in hospital outpatient clinics as well as private practices who participated in the Lilly Germany database (about 5000) were addressed and asked to take part in the afore-mentioned study. About 20% were primarily interested in participating. In these 693 centers, patients were actively enrolled. Only adult outpatients with a minimum age of 18 years, clinical signs and symptoms of depressive episodes (according to ICD-10 criteria) who intended to start treatment with the antidepressant duloxetine were included in the study. Patterns of treatment, treatment initiation or corresponding changes were at the discretion of the physicians and the patients, according to the usual standard of care. Moreover, the indication for prescribing and inclusion in the observational study were at the full discretion of the physician. Regarding the study medication, it was not provided by the sponsor.

Between 2005 and 2007, 4517 outpatients with an acute depressive episode were treated with duloxetine (flexible doses: 30–120 mg/day) for 6 months by psychiatrists or neurologists. Outcome variables were: self-rated visual analogue scales (VAS) for mood, activity, tension/relaxation, sleep, appetite (“Kurzskala Stimmung/Aktivierung” (KUSTA [4])) (daily assessments in the first 4 weeks) and for several forms of pain (daily assessments in the first 4 weeks); the physician-rated somatic symptom inventory (SSI) [2] and also the physician-rated inventory for depressive symptomatology-clinician rated version (IDS-C) [11]. Rater training was not performed in the context of this naturalistic study. However, several quality assurance measures have been implemented including a data validation plan with plausibility checks and double data entry. Physicians arrived at a clinical diagnosis on the basis of ICD-10 criteria.

All patients gave written informed consent according to the guidelines of the Declaration of Helsinki. The study was approved by the relevant local research ethics committee.

Each patient was asked about the length of time until their current depressive episode had developed to full severity using pre-defined time categories (Fig. 1). Furthermore, it was recorded whether acute critical life events or permanent stressors preceded the onset of the current depressive episode.

A cut-off score of 1 week for the speed of onset of the depressive episode was chosen since this score separated patients with unipolar and bipolar depression very well [8].

In order to reduce factors which may have had confounding effects with respect to the reported speed of onset, 831 patients with an acute critical life event preceding the current depressive episode (e.g., interpersonal conflicts, work-related critical life events like loss of work, death of close relatives, daily stressors like relocation) as well as 1003 patients with comorbid panic disorder as measured by a baseline IDS-C score for item 27 (“panic/phobic symptoms”) of two or more were excluded. The latter group was excluded because some patients might confuse the panic attack with the onset of the depressive episode; however, patients with a diagnosis of anxiety disorders and/or obsessive-compulsive disorder were not excluded. Forty-seven patients were excluded because of missing values. The final sample consisted of 2636 patients. In Fig. 1, the frequency distribution of the speed of onset of the depressive episode is shown.

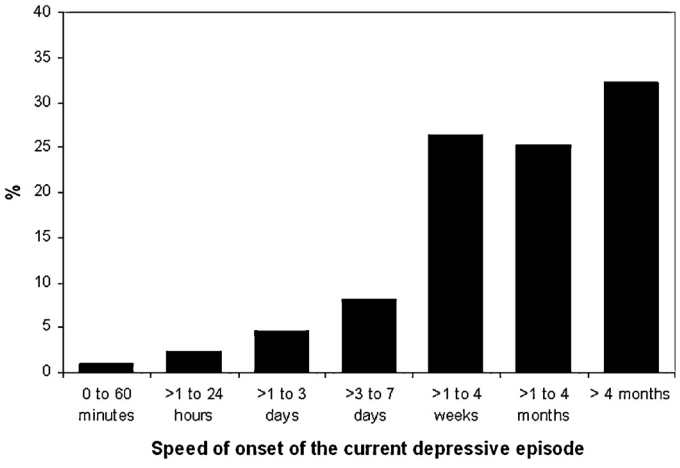

Fig. 1. Frequency distribution of the speed of onset of the current depressive episode in the sample.

2.2. Data analysis

Data were analyzed by SAS (version 9.1). Group differences in normally distributed data were analyzed by using *t* tests for independent sample comparison and differences in data sets with non-normal distribution (according to the folded f-statistic to test for equality of variances) by the Mann-Whitney test. Binary and categorical data were analyzed by Fisher’s exact and Chi-square tests respectively. The significance level was set at two-sided $\alpha = 0.05$.

Additionally, we used binary logistic regression to model the odds of having a speed of onset of the current depressive episode of more than 1 week (slow onset of depression). The baseline variables included:

- demographic variables:
  - age,
  - sex,
  - employment,
  - living alone;
- clinical variables:
  - attempted suicide in the last year,
  - any concomitant somatic diseases,
  - age at onset of depression,
  - IDS-C6 total score at baseline [3] in order to assess the core items of depressive disorders (IDS-C [11] items 1, 5, 7, 16, 20, 23),
  - pain (no pain, organic pain, non-organic pain),
  - any permanent pain medication,
  - hospitalization in the last year,
  - anxiety disorders/obsessive-compulsive disorders,
  - KUSTA mood score at baseline.

Binary logistic regression analysis was performed with fast versus slow onset (≤ 7 days versus > 7 days) of the depressive episode as the dependent variable, starting with all independent variables in the model and then removing the least statistically significant variables one at a time until only variables showing a significant correlation ($P \leq 0.05$) with the outcome remained. For these variables, Wald Chi-square *P* values, odds ratios (OR) and their 95% confidence intervals (CI) are reported. Forward, backward and stepwise logistic regressions were also performed with $P < 0.10$ as the entry and elimination threshold to confirm the model.

In order to explore the association between the speed of onset of the current depressive episode and time to mood response, a subgroup analysis was performed for patients with a greater than median improvement of KUSTA mood at day 27. For each patient, the earliest diary day for each KUSTA mood on which 50% of the patient’s improvement between days 0 and 27 was achieved was then calculated to determine individual “time to 50% mood response”. In a next step, the association of this parameter with the