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Research report

Association between symptomatic profile and remission following antidepressant treatment in unipolar major depression

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ABSTRACT

Background: To evaluate, in patients affected by an acute major depressive episode, what predictive value certain baseline psychopathological characteristics have with regard to expected therapeutic remission following biological antidepressant treatment (pharmacological/electroconvulsive; non-psychological).
Methods: Six predefined psychopathological characteristics in acute major depressive episode were evaluated using a logistic regression model through a protocolised antidepressant treatment to assess their predictive value with regard to expected remission rate.
Results: The final study sample consisted of 129 subjects affected by an acute major depressive episode. From the baseline evaluation of the anguish/restlessness, reduced emotional reactivity, reduced attention, reduced motor response, feeling of worthlessness, and mood characteristics items, it was possible to correctly classify 88.1% of the sample as remitter/non-remitter with sensitivity of 0.77 and specificity of 0.96. Addition of the 17-item HRSD baseline variable to the regression model increased the capacity for correct classification of the baseline sample by only 0.09%.
Limitations: Protocolised antidepressant treatment was used. The results of this study may not be generalisable to pharmacological treatments not included in this protocol.
Conclusions: The results of this study suggest that certain baseline psychopathological characteristics (and perhaps other clinical variables too) of the acute major depressive episode may be of great use in establishing patient subgroups according to expected clinical remission to the administration of biological antidepressant treatment. This could have considerable consequences for individualised therapeutic decision-making and for future researches (clinical trials included).

1. Introduction

The absence of contrasting prognostic biomarkers which allow us to individualise and optimise treatment of depressive syndrome, invites investigation of the possibility that the psychopathological characteristics themselves may be of great use in individualised therapeutic decision-making (Copenhagen Marriot, 2007). Both the revision of the published bibliography (Buyukdura et al., 2011; Spijker et al., 2001; Uher et al., 2011) and clinical practice suggest that diverse psychopathological characteristics of the acute major depressive episode could provide very useful information with respect to the probability that this major depressive episode represents clinical remission or otherwise following administration of the appropriate biological treatment (pharmacological and/or electroconvulsive).

The aim of this study was to evaluate, in patients affected by an acute major depressive episode, what predictive value diverse baseline psychopathological characteristics have on expected clinical remission/non-remission following protocolised biological antidepressant treatment. The hypothesis formulated for this study was that certain psychopathological characteristics of the acute major depressive episode (in particular, anguish/restlessness, reduced emotional reactivity, reduced attention, reduced motor response, feeling of worthlessness, and mood characteristics) allow reasonably reliable prediction of the probability of clinical remission following prescribed biological antidepressant treatment. Specifically, we suggest that the greater the clinical intensity of these symptoms, the greater the probability of clinical remission through biological antidepressant treatment.

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2. Methods

2.1. Sample

This study was carried out in Hospital Clínic, Barcelona. All consecutive ambulatory and hospitalised patients seen between September 2009 and September 2011 with a diagnosis of unipolar depressive disorder and aged over 17 years were included. All met DSM-IV criteria (American Psychiatric Association, 1994) for acute major depressive episode. Those patients with a history of hypomania, mania or non-affective psychosis were excluded from the study.

Following an exhaustive study description, all patients were required to provide informed consent prior to participation. Where there was doubt with respect to the patient's capacity to understand, consent was also requested from a close family member.

2.2. Clinical assessment

With the aim of defining the clinical characteristics of the patient sample, depressive symptomatology was quantified through the Spanish version of 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960; Ramos-Riviera and Cordero-Villafafila, 1988). Sub-classification of psychotic versus non-psychotic was determined through the presence or otherwise of delusions at baseline assessment. Evaluation of delusions was carried out through in the clinical interview.

Together with the symptomatic evaluation obtained through the 17-item HRSD, we performed a detailed assessment of the psychopathological items which, according to the study hypothesis, would be of greatest relevance in predicting remission: anguish/restlessness, reduced emotional reactivity, reduced attention, reduced motor response, feeling of worthlessness, and mood characteristics. Selection of these items was based on the revision of the published bibliography (Buyukdura et al., 2011; Spijker et al., 2001; Uher et al., 2011) and, in particular, on our group's clinical experience. To evaluate and quantify these psychopathological characteristics, we used the scheme described in Table 1, which we denominated Prediction Assessment of Remission for Unipolar Depression (PARUD). Each of the 6 psychopathological characteristics was evaluated on scores ranging from 0 to 3 (from lower to higher intensity) and from the total of individual scores a global value was obtained (between 0 and 18). According to the formulated hypothesis, a higher global score on the PARUD would indicate a greater probability of remission following protocolised, biological, antidepressive treatment.

Remission was defined as obtained, in two consecutive visits and according to two separate assessors, a score of less than 8 on the 17-item HRSD. Similarly, to be considered as being in remission in the case of episodes with baseline psychotic symptoms, these symptoms should be fully resolved in each of these two visits.

2.3. Study design

This is a longitudinal study. At baseline visit, subjects' demographic and clinical data were collected and the 17-item HRSD and PARUD were administered along with evaluation of the presence or otherwise of psychotic symptomatology. Once this information had been gathered, treatment with the appropriate biological antidepressant began. The second and third visits were conducted fortnightly and, from then on, monthly until completion of clinical follow-up (with the proviso that each time a new antidepressant treatment was carried out, the two subsequent visits were conducted on a fortnightly basis). The 17-item HRSD and the PARUD were administered each month and presence of psychotic symptomatology was assessed.

2.4. Treatment protocol

The treatment prescribed to patients was adjusted in line with that established in our hospital's Unipolar Depression Unit Clinical Guide. This Clinical Guide is essentially structured according to the PARUD baseline score. When the baseline PARUD score is $\leq$6 the initial treatment proposed is a selective serotonin reuptake inhibitor (SSRI), specifically, fluoxetine (20–40 mg/day) or escitalopram (15–30 mg/day); for scores between 7 and 12, the initial proposed treatment is venlafaxine extended-release (225–300 mg/day) and for patients with scores higher than 12, initial treatment is a tricyclic antidepressant (TCA); specifically, imipramine or nortriptyline (dose based on plasma levels). In this last case, an option also permitted by our Clinical Guide is electroconvulsive therapy (ECT). ECT is only prescribed without a previous failed attempt (due to inefficacy or intolerance) at pharmacological treatment with TCAs, if the patient presents great agitation or an absolute refusal to ingest food or liquids.

According to the Clinical Guide, following four weeks of treatment with the prescribed pharmacological option (and a minimum of 4 weeks at therapeutic dose or within the therapeutic window), in the case of favourable outcome the prescribed therapeutic option is maintained (with optional increase of dosage). Favourable outcome is defined as a reduction of a minimum of 4 points on the PARUD or, if the PARUD score is 0, of a minimum of 8 points on the 17-item HRSD. In the case of absence of clinical improvement or clinical improvement without complying with what we have defined as favourable outcome, treatment moves to the next therapeutic step. The change in treatment is carried out over approximately 4 days when consists of the substitution of fluoxetine or escitalopram for venlafaxine extended-release, and in approximately 7–10 days, substitution of venlafaxine extended-release for imipramine or nortriptyline.

In cases where ECT is chosen, this is administered three times per week with a constant current, brief pulse device. Although there is increasingly abundant bibliography suggesting that twice weekly is just as effective as thrice weekly (Charlson et al., 2012), for the moment thrice weekly administration continues to be our clinical practice. Using a systematic protocol, all treatment stimuli are delivered with frontotemporal electrode placement administered using a MECTA-SR2 ECT device. The seizure threshold is titrated at treatment 1. Electroencephalographic and motor seizure manifestations are monitored to ensure adequate duration. Succinylcholine (40–100 mg), atropine (0.5–1 mg), and thiopental (200–300 mg) are used for anaesthesia. Acute ECT is continued until patients are remitters or show no further improvement over the course of three consecutive treatments. In our Clinical Guide, each doctor may decide whether or not to combine this with pharmacological antidepressant treatment. In this study, patients who did not obtain clinical remission following ECT were considered non-remitters.

Concomitantly with pharmacological antidepressant treatment or with ECT, the patients may receive symptomatic treatment with hypnotics (lormetazepam) or anxiolytics (clonazepam or lorazepam) or, in the presence of very intense anxiety symptomatology, with olanzapine. In addition, in the case of the presence of psychotic symptoms, the antidepressant pharmacological treatment is combined with risperidone (or, on rare occasions, with haloperidol).

In our hospital's Clinical Guide, psychological treatment is recommended as monotherapy or in combination with biological antidepressant treatment in certain clinical profiles (PARUD$\leq$6). However, in this study, this therapeutic option was excluded. This