CLINICAL PREDICTORS OF ANTIDEPRESSANT RESPONSE AND REMISSION IN TREATMENT RESISTANT DEPRESSION

Raffaella Calati 1, Daniel Souery 2, Isabelle Massat 3, Siegfried Kasper 4, Stuart Montgomery 5, Joseph Zohar 6, Julien Mendlewicz 7, Alessandro Serretti 1

1 University of Bologna, Institute of Psychiatry, Bologna, Italy
2 Laboratoire de Psychologie Médicale, Université Libre de Bruxelles, and Centre Européen de Psychologie Médicale-PsyPluriel, Brussels, Belgium
3 Université Libre de Bruxelles, Fonds de la Recherche Scientifique (FNRS) Laboratoire de Neurologie Expérimentale, Brussels, Belgium
4 Medical University of Vienna, Department of Psychiatry and Psychotherapy, Vienna, Austria
5 University of London, Imperial College, London, United Kingdom
6 Chaim Sheba Medical Center, Chaim Sheba Medical Center, Tel-Hashomer, Israel
7 Université Libre de Bruxelles, Brussels, Belgium

ABSTRACT

AIM: The aim of this study was to identify predictors of antidepressant response/remission in Treatment Resistant Depression (TRD) prospectively assessed patients and to compare results to ones obtained in a previous study on TRD patients retrospectively assessed (1).

METHODS: 417 patients who failed to respond to a previous antidepressant were firstly included in a 6-week treatment with venlafaxine; secondly, those who failed to respond were treated for a 6-week treatment with escitalopram. MINI, HRSD, MADRS, CGI-S and CGI-I were administered.

RESULTS: In the first phase, non responders and non remitters to venlafaxine main features were higher rate of side effects, higher baseline CGI-S and higher current suicidal risk level. In the second phase, non responders and non remitters to escitalopram reported higher duration of current episode, higher baseline CGI-S, higher rate of current suicidal risk, higher rate of comorbid anxiety disorders and higher rate of antecedents of second degree affected by bipolar disorder.

CONCLUSIONS: Some clinical variables have been identified as associated with treatment non response/non remission in TRD. They could guide clinicians to a more aggressive treatment when present.

BACKGROUND

Despite the available effective pharmacotherapeutic strategies, only 30-40% of patients affected by Major Depressive Disorder (MDD) respond to the first adequate – in terms of dosage and duration – antidepressant. The remaining non responder patients (60-70%) could be defined as Treatment Resistant Depression (TRD) patients.

However, different definitions of TRD have been suggested (2): from the lack of response to 1 antidepressant, to the lack of response to 2 or more antidepressants of different classes.

Numerous studies reported factors predicitive of treatment response to a single antidepressant (psychiatric and somatic comorbidities, family history, psychosocial factors) but multiple failures in the same episode have been poorly investigated in terms of clinical predictors.

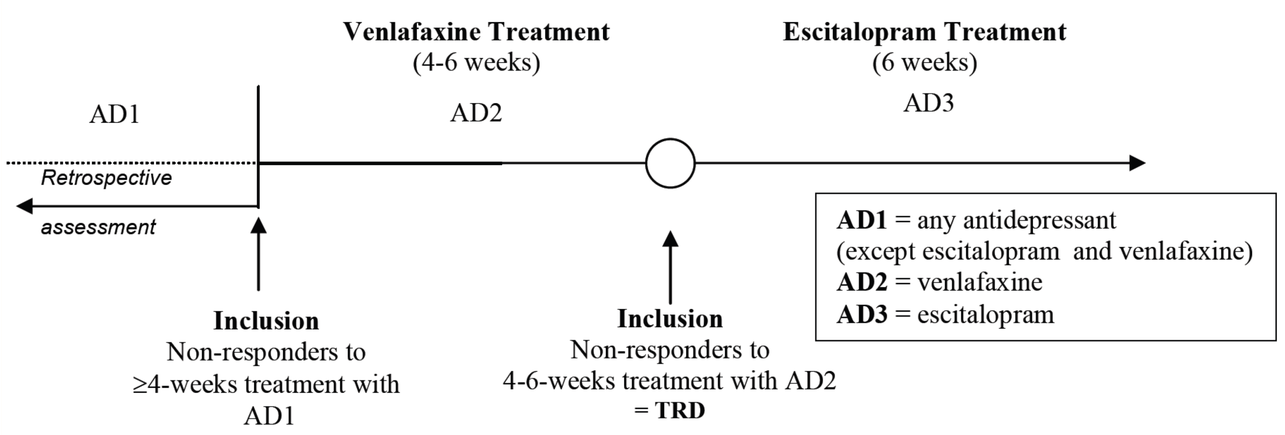
Some clinical features were found to be associated with TRD to 2 consecutive adequate antidepressant treatments: anxiety comorbidity, comorbid panic disorder and social phobia, personality disorder, suicidal risk, severity, melancholia, number of hospitalization >1, recurrent episodes, early age at onset, non response to the first antidepressant received lifetime (1).

AIM OF THE STUDY

The aim of this study was: 1) to identify clinical predictors of antidepressant response/remission in a sample of TRD prospectively assessed patients having received 2 or more antidepressant treatments, and 2) to compare the obtained results to the ones previously obtained on another sample of TRD patients retrospectively assessed (1) in the context of the same European multicenter project "Patterns of Treatment Resistance and Switching Strategies in Affective Disorder", carried out by the Group for the Study of Resistant Depression (GSRD).

METHODS

The study design scheme is given below:



Sample

A sample of 417 MDD patients (mean age: 47.0±12.5 years; males: 33.0%; Caucasians: 93.0%) was prospectively assessed. Included patients must: 1) be non responders to at least 1 adequate antidepressant treatment (except venlafaxine or escitalopram), 2) have a Current Major Depressive Episode, moderate or severe according to DSM-IV-TR criteria, 3) have a total score ≥22 at the Montgomery and Asberg Depression Rating Scale (MADRS). Patients were excluded if: 1) they were non responders to a combination of 2 antidepressants, 2) they have any current psychiatric disorder other than MDD as a principal diagnosis, 3) they received not allowed treatments (benzodiazepines – more than 25mg/day of diazepam or equivalent within the last week, antipsychotics, mood stabilizers, ECT within the past 6 months, formal psychotherapies started in the month preceding inclusion).

Assessment and statistical analyses

The Mini International Neuropsychiatric Interview (MINI) was administered at baseline. MADRS, Hamilton Rating Scale for Depression (HRSD), Clinical Global Impression Severity (CGI-S) and Improvement (CGI-I) scales were administered from baseline to week 12. Other information has been collected at baseline, such as socio-demographic features, psychiatric antecedents and previous treatments.

Statistical analyses on responders and remitters at the endpoints of the study were performed using Chi2, Student t test and stepwise regression.

RESULTS

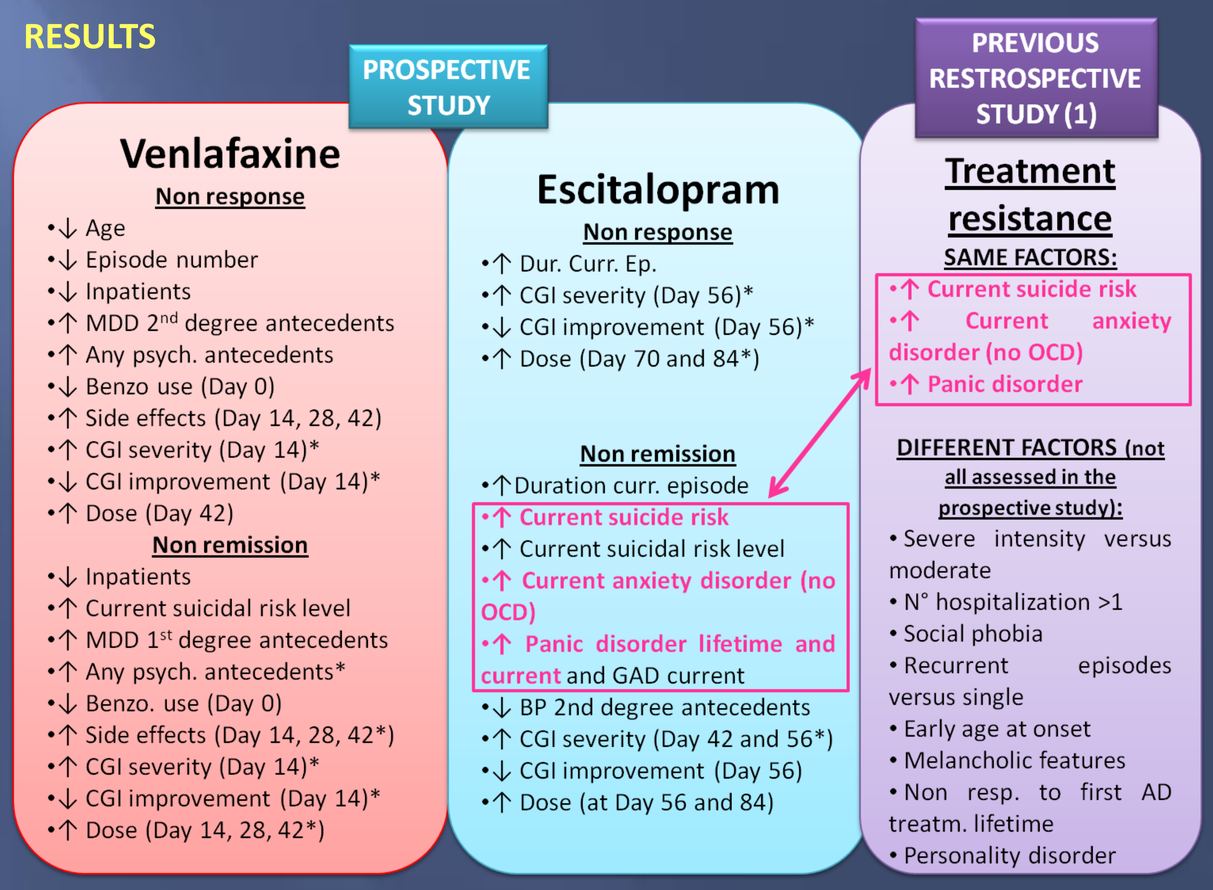


Figure - Variables associated with treatment response-remission to venlafaxine and escitalopram versus variables associated with treatment resistance in a previous retrospective study on an independent MDD sample (1).
*p≤0.0001

CONCLUSIONS

Through the present investigation some clinical variables have been identified as associated with treatment non response/non remission in TRD. If we compare these findings with the ones previously reported by the same group (GSRD) in a retrospective investigation on an independent sample (1), we find some similarities: specifically, current suicidal risk and comorbid anxiety disorders, in particular panic disorder, seem to be predictors of treatment non remission/resistance in two sample of TRD patients, prospectively and retrospectively followed. However, the issue of selection of patient subgroups after each failure should be considered when interpreting features associated with each step resistance.

This poster is financially sponsored by Lundbeck A/S and the Belgian National Fund for Scientific Research (FNRS; 3.4.530.07 F). Dr. Serretti is or has been consultant/speaker for: Abbott, Angelini, Astra Zeneca, Clinical Data, Boheringer, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Lundbeck, Pfizer, Sanofi, Servier. Dr. Kasper: Eli Lilly, Lundbeck, Bristol-Myers Squibb, GlaxoSmithKline, Organon, Sepracor, Servier; AstraZeneca, Pfizer, Schwabe, Janssen, Novartis and Pierre Fabre. Professor Montgomery is or has been consultant/speaker for: AstraZeneca, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Lundbeck, Merck, Merz, Neurim, Pierre Fabre, Pfizer, Sanofi, Servier, Shire, Sepracor, Takeda, Targacept, Wyeth, Bionevia, M's Science, Otsuka, Pharmaneuroboost, Richter, Roche, Theracos, Transcept, UBC and Xytis. Other Authors have no potential conflict of interest.

REFERENCES

1. Souery, D., et al., Clinical factors associated with treatment resistance in major depressive disorder: results from a European multicenter study. J Clin Psychiatry, 2007. 68(7): p. 1062-70.
2. Berlim, M.T. and G. Turecki, What is the meaning of treatment resistant/refractory major depression (TRD)? A systematic review of current randomized trials. Eur Neuropsychopharmacol, 2007. 17(11): p. 696-707.