P.3.009

Polypharmacy in a naturalistic cohort study of bipolar patients: A principal component analysis of treatment patterns according to clinical features.

Alessandra M.A. Nivoli [1,2], Francesc Colom [1], Isabella Pacchiarotti[1], Andrea Murru [1], Marc Valenti [1], Barbara Patrizi[1], José Sanchez-Moreno [1], Eduard Vieta [1]

[1] Bipolar Disorders Programme, Institute of Clinical Neuroscience, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain;

[2] Unit of Psychiatry, Department of Neurosciences, University of Sassari, Italy;

BACKGROUND

In clinical practice no fixed approaches exist on how to treat a patient with bipolar disorder. Despite the existence of several treatment guidelines, clinicians employ different criteria in their decision-making process and factors that predict physician's decisions have not been studied in detail (Hoblyn et al., 2006). Furthermore, it is not known which combinations treatment are most common and which patients are mostly likely to receive these medication combinations (Mojtabai 2010).

OBJECTIVE

The aim of our study is to identify the more frequent combination strategies for the treatment of patients with bipolar disorder within clinical practice and to detect clinical factors that predict physician's treatment approaches.

METHODS

We propose a principal component analysis (PCA) approach to identify the most frequent patterns of treatment combinations in bipolar out-patients enrolled in a naturalistic cohort study. Medication options were classified in 15 options (see table 1) including all medications taken during life-spam. The PCA analyses the total variance of the selected treatment options and reduce them into fewer uncorrelated factors that capture most of the information. Once factors have been extracted, univariate analyses were performed in order to find clinical characteristics of patients accounting for each group using each factor as a dichotomic variable (YES/No). Logistic regression models were then employed to quantify the impact of every independent variable on the outcome for each factor. Multivariate analyses were used to detect difference between the factors: the ANOVA for continuous variables with post-hoc procedures (Bonferroni correction) and Pearson Chi-square (or Fisher's exact test when frequency <5) in contingency tables ($\chi 2$), for categorical. The Kolmogorov-Smirnov statistic was used to test the normality of distributions. Mean differences in quantitative variables with a non-normal distribution were assessed by using the Kuskal-Wallis test for independent groups. Significance was set at p<.05 (two tailed). Statistical analyses were performed using SPSS, 16.0 version for Windows.

RESULTS

The sample was composed by 604 bipolar patients, 272 men (45%) and 332 women (55%). Three clearly interpretable and clinically relevant factors were identified, with the same numbers of Eigen values confirmed by the inflection point at the Scree plot. Altogether they capture the 57.8% of the rotated variance (table 1). The first, strongest factor, capturing alone the 21.1% of rotated variances, named ***Antimanic stabilization Package,*** groups prescriptions of Mood stabilizers-Atypical Antipsychotics-ECT with significant positive loading for lithium, valproate, carbamazepine, clozapine, risperidone, olanzapine and electro convulsive therapy (ECT). The second one, capturing the 20.4% of rotated variance, represents prescription of LMT-Atypical antipsychotics, with significant positive loading for lamotrigine, quetiapine, aripiprazole and ziprasidone, defined ***Antidepressant stabilization package***. The third component (16.4% of rotated variance) comprises the use of ADs alone, with significant loading for TCAs, IMAOs, SSRIs and SNRIs, defined as ***Anti-bipolar II package***.

Table. 1 Component Matrix: rotated factor loadings for lifetime drug prescriptions

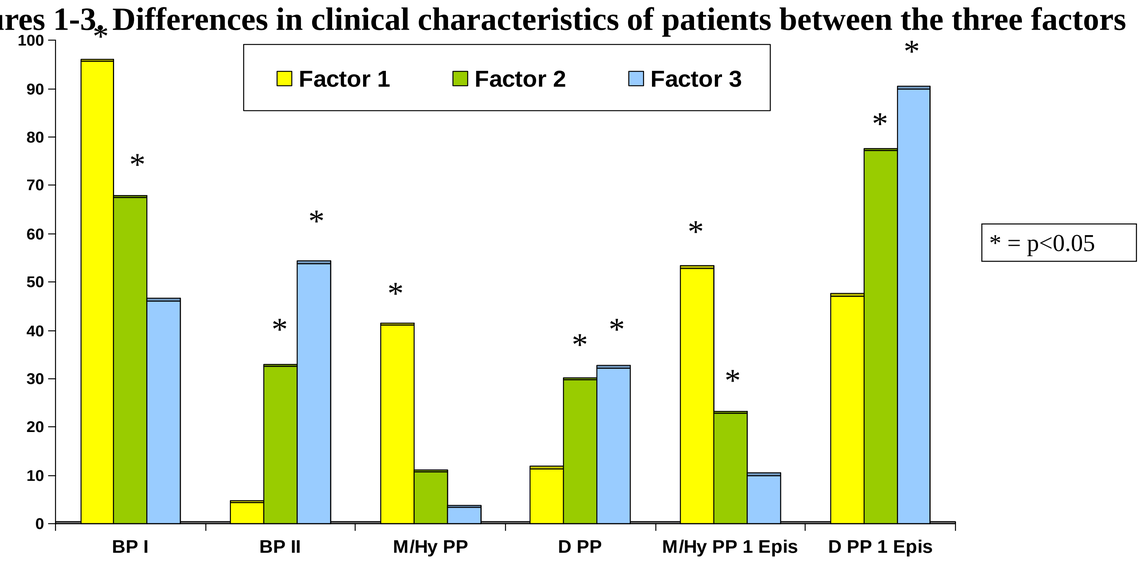
	Factors		
Drug prescriptions	**1**	**2**	**3**
Lithium	.494		
Carbamazepine	.592		
Valproate	.393		
Lamotrigine		.736	
Tricyclic Antidepressants			.738
Monoamine Oxidase Inhibitors			.611
Selective Serotonine Reuptake Inhibitors			.702
Serotonine and Noradrenaline Reuptake Inhibitors			.662
Clozapine	.737		
Risperidone	.698		
Olanzapine	.627		
Ziprasidone		.778	
Quetiapine		.771	
Aripiprazole		.803	
Electro Convulsive therapy	.656		
Variance (total: 57.8%)	**21.1%**	**20.4%**	**16.4%**

Normalization with Varimax rotation. Multicollinearity was excluded (determinant >.0001); KMO and Barret's test (p<.05). Eigen values greater than 0.9. were considered. Items loadings with absolute values greater than 0.32 were used to describe the factors and confirmed by the scree plot cutoff point.

Factor 1 is characterized by the majority of patients being diagnosed with a Bipolar I disorder (95.7%, $\chi 2$ =44.220, p<0.001), with manic/hypomanic predominant polarity of the course of illness (41.1%, $\chi 2$ =44.273, p<0.001) and at first episode (52.9%, $\chi 2$ =35.392, p<0.001), more psychotic symptoms during the course of illness (88.4%, $\chi 2$ =51.207, p<0.001) and psychotic depression (42.6%. $\chi 2$ =17.117, p<0.05). Age at illness onset is significantly earlier (23.1, SD 8.3, F=6.890, p<0.001), as well as the age at first hospitalization (27.9, SD 11.6, F=8.296, p<0.001), with significantly more hospitalizations (3.7, SD 3.1; F=16.796, p<0.000), more manic (5.2, SD 5.1, F=14.910, p<0.001) and mixed episodes (1.6, SD 3.06; F=6.565, p<0.001).

Factor 2 is characterized by the presence of more patients with BPI rather than BPII (67.5% vs 32.5%) with a predominant polarity significantly more depressive than manic/hypomanic (29.8% vs 10.7%, $\chi 2$ =44.273, p<0.001) and with depressive onset of illness (77.2%). These patients seemed to be significantly more sensitive to stressors (life events, 85.7%, $\chi 2$ =16.602, p<0.001) compared to the other two groups. **Factor 3** was characterized by the majority of patients being diagnosed with a BPII (53.9%, $\chi 2$ =46.979, p<0.001) with a significant prevalence of predominantly depressed patients (32.2%, $\chi 2$ =10.263, p<0.05) and a depressive onset (90.0%, $\chi 2$ =35.392, p<0.001). The course of the illness appeared to be characterized by the significant presence of melancholic features (50.0%, $\chi 2$ =13.991, p<0.05) and a high frequency of suicide ideation (74.4%), significantly more number of total episodes (20.6, SD 25.2, F=4.760, p<0.005), particularly hypomanic (7.9, SD 12.2, F=4.689, p<0.005) and depressive episodes (11.8, SD 14.65, F=5.831, p<0.001).

Figures 1-3. Differences in clinical characteristics of patients between the three factors



CONCLUSIONS

To the best of our knowledge this is the first study using this factorial approach to analyze complex treatment approaches in order to define the most frequent patterns of combination treatment in bipolar disorder and their relationship to clinical features of patients within clinical practice. The *Antimanic stabilization Package* includes the use of mood stabilizers and antipsychotics with a strong action on positive and psychotic symptoms, and ECT, usually used for resistant patients. Patients are BPI with a clear manic/hypomanic predominant polarity of the course of illness and at onset, with psychotic features, earlier onset and early age at first hospitalization, high number of hospitalizations, numerous manic and mixed episodes, with a bad adherence to treatment and low personal autonomy. Patients treated with the *Antidepressant stabilization Package*, which include drugs with clear action on depressive features (lamotrigine and quetiapine) and also antimanic (ziprasidone and aripiprazole) were also BPI but they presented with a predominant polarity significantly more depressive than manic/hypomanic with a polarity at onset both depressive and manic/hypomanic. These patients seemed to present a more changeable clinical presentation and to be significantly more sensitive to stressors life events. Patients treated with the *Anti-bipolar II package* , which includes the use of antidepressants, were BPII with a significant prevalence of predominantly depressed patients, a depressive onset, with melancholic features, more number of depressive episodes.

REFERENCES

Mojtabai R, Olfson M. National trends in psychotropic medication polypharmacy in office-based psychiatry. Arch Gen Psychiatry. 2010 Jan;67(1):26-36. Hoblyn J, Noda A, Yesavage JA, Brooks JO 3rd, Sheikh J, Lee T, Tinklenberg JR, Schneider B, O'Hara R, Leslie DL, Rosenheck RA, Kraemer HC. Factors in choosing atypical antipsychotics: toward understanding the bases of physicians' prescribing decisions. J Psychiatr Res. 2006 Mar;40(2):160-6.