

CLINICAL IMPLICATIONS OF PREDOMINANT POLARITY AND THE POLARITY INDEX OF DRUGS IN MAINTENANCE TREATMENT OF BIPOLAR DISORDER: A NATURALISTIC STUDY

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PURPOSE OF THE STUDY

Predominant polarity, defined as at least twice as many episodes of one pole over the other, is among the strongest predictors of recurrence into a specific episode in Bipolar Disorder (BD), and should be considered when implementing maintenance therapy. Our group has recently developed the Polarity Index (PI), a metric indicating antimanic versus antidepressive potential of drugs [1]. The purpose of this study was to determine the role of PI in clinical decision-making. Secondary aim was to assess differences between predominantly manic and depressed patients, with a special focus on their pharmacological treatment.

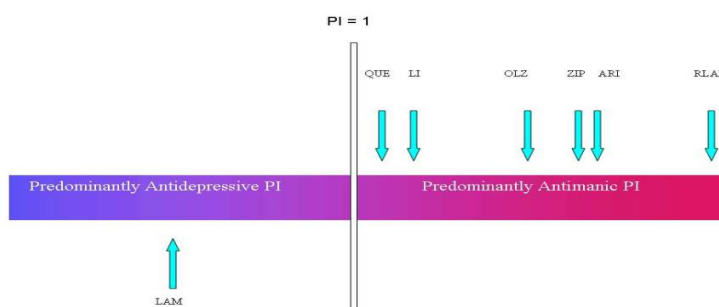
METHODS

The study sample was composed of 604 patients aged ≥ 18 , with BD I or II, who signed an informed consent, enrolled in the systematic prospective follow up study of the Bipolar Disorders Program of the Hospital Clinic of Barcelona, Spain. Patients who fulfilled criteria for either Manic (MPP) or depressive (DPP) were compared regarding socio-demographic, clinical and therapeutic characteristics.

The PI, a numeric expression of the efficacy profile of a given drug, derives from Number Needed to Treat (NNT) for prevention of depression and NNT for prevention of mania ratio, as emerging from the results of randomized placebo-controlled trials [1, 2]. Drugs with $PI > 1$ have stronger antimanic prophylactic properties, while those with $PI < 1$ are more effective for preventing depressive episodes than the manic ones. The PI of drugs for maintenance treatment of BD was: 12.09 for risperidone, 4.38 for aripiprazole, 3.91 for ziprasidone, 2.98 for olanzapine, 1.39 for lithium, 1.14 for quetiapine, and 0.40 for lamotrigine [1]. PI for patients' current treatment was calculated as mean value of all prescribed drugs in each patient.

Drug	NNT Mania	NNT Depression	NNT Any Mood Episode	Polarity Index
Aripiprazole ^{1,2}	8.81	38.55	6.6	4.38
Lamotrigine ^{12,13}	50.4	20.2	11.6	0.40
Lithium ^{8,12,13,14,15}	4.4	6.1	3.5	1.39
Olanzapine ^{3,4,5}	4.7	14	3.5	2.98
Oxcarbazepine ¹⁶	8.2	5.1	5	0.62
Quetiapine ^{6,7,8}	3.5	4	2.8	1.14
Risperidone LAI ^{5,9,10}	4.4	53.2	4.5	12.09
Valproate ¹⁵	21.3	10.5	7	0.49
Ziprasidone ¹¹	14.1	55.1	7.8	3.91

LAI=Long-acting Injection;¹Keck et al., 2007; ²Marcus et al., 2011; ³Tohen et al., 2006; ⁴Tohen et al., 2004; ⁵Vieta et al., 2012; ⁶Vieta et al., 2008a; ⁷Suppes et al., 2009; ⁸Weisler et al., 2009; ⁹Quiroz et al., 2010; ¹⁰Macfadden et al., 2009; ¹¹Bowden et al., 2010; ¹²Bowden et al., 2003; ¹³Calabrese et al., 2013; ¹⁴Prien et al., 1973; ¹⁵Bowden et al., 2000; ¹⁶Vieta et al., 2008b



We declare no conflict of interests for this study

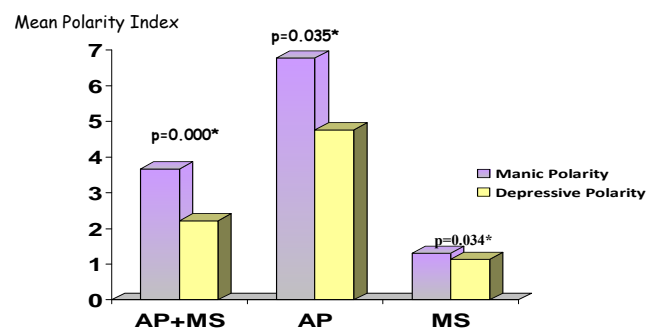
RESULTS

257/604 (43%) of patients with BD-I or II fulfilled criteria for manic (MPP) or depressive PP (DPP). 143 patients (55.6%) fulfilled criteria for DPP and 114 (44.4%) for MPP.

Total PI, as well as Antipsychotics' PI and Mood Stabilizers PI were higher, indicating a stronger antimanic action, in MPP (Table 1).

MPP presented higher prevalence of BD-I, male gender, younger age, age at onset and at first hospitalization, more hospitalizations, primary substance misuse and psychotic symptoms. DP correlated with BD-II, depressive onset, primary life events, melancholia and suicide attempts. The prescription of First Generation Antipsychotics and Second Generation Antipsychotics Olanzapine and Risperidone was significantly more frequent among MPP patients, whilst use of Lamotrigine, Selective Serotonin Reuptake Inhibitors, Serotonin-Norepinephrine Reuptake Inhibitors, Tricyclic Antidepressants and Benzodiazepines was more prevalent amongst DPP patients.

	Manic Polarity (n=114)		Depressive Polarity (n= 143)		Mann-Whitney U	p	Kolmogorov-Smirnov Z
	Mean	SD	Mean	SD			
Polarity Index AP+MS	3.68	3.19	2.22	2.36	3385.5	0,000*	2.069
Polarity Index AP	6.78	4.68	4.77	4.53	1281.5	0,006*	1.425
Polarity Index MS	1.31	0.23	1.14	0.38	2679.0	0,001*	1.429



AP= Antipsychotics
MS= Mood Stabilizers

CONCLUSIONS

The results of this naturalistic study confirm the usefulness of the PI. In this large sample, clinical differences among these groups justify differential treatment approach. The PI appears to be a useful way to operationalize what clinicians do for maintenance therapy in BD.

REFERENCES

- [1] Popovic, D., Reinares, M., Goikolea, J.M., Bonnín, C.M., Gonzalez-Pinto, A., Vieta, E., 2012. Polarity Index of Pharmacological Agents used for Maintenance Treatment of Bipolar Disorder. Eur Neuropsychopharmacol. 22(5), 339-346.
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