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Letter to the Editor

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Serum lithium levels are associated with white blood cell counts in bipolar disorder

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To the Editor

Blood cells in circulation could be disturbed both qualitatively and quantitatively in psychiatric disorders. Previous studies have reported alterations in the number (1,2) and function (3) of blood cells in psychiatric disorders. Alterations might be related to different etiologies in different psychiatric disorders (1) and medications (4,5). After the reversal of these mechanisms by successful treatment with escitalopram, the platelet volumes were normalized in first episode, medication-naïve patients with major depressive disorder (6). In bipolar disorder, mood stabilizers seem to be the major reason for the changes in blood cells (4,5). In patients with psychotic spectrum disorders, the mean platelet volume (MPV) is increased, especially in patients on atypical antipsychotics (7).

We have analyzed the blood cell counts of outpatients in our clinic between 1 January, 2012 and 31 December, 2014. Major depressive disorder (n = 338), bipolar disorder (n = 389), and psychotic spectrum disorders (n = 227) were the diagnostic groups examined in our analysis. The results of the comparison between the groups are presented in Table 1. These results confirm the previous study results, which reported increased leukocytes and decreased erythrocytes and platelets in bipolar disorder.

Lithium (Li) increases the number of leukocytes in circulation (4,8–10). We further compared hematological parameters in patients on Li (n = 124), patients on valproate (VPA) (n = 203), and patients not taking a mood stabilizer (n = 51) in the bipolar disorder group (Table 2). Since Li and VPA have similar mechanisms of action, we proposed that VPA might also have effects similar to those of Li. However, there were differences in the platelet distribution width (which was higher in VPA-treated patients than in mood stabilizer-free patients with bipolar disorder, P = 0.006), platelet counts (which were lower in VPA-treated patients than in Li-treated patients (P = 0.000002) and mood stabilizer-free patients with bipolar disorder (P = 0.040)), WBCs (which were lower in VPA-treated patients than in Li-treated patients, P = 0.000076), and red blood cell counts (which were lower in VPA-treated patients

Table 1. Demographics and hemogram parameters in the groups.

	Bipolar disorder (n = 389)	Major depression (n = 338)	Psychotic spectrum disorders (n = 227)	χ^2/F	P
Age	42.07 ± 13.60	46.69 ± 16.85	41.59 ± 14.03	11.31	**0.000014**
Sex (f/m)	227/162	228/110	110/117	23.44	**0.000103**
PLT	247.30 ± 67.30	260.03 ± 66.66	249.08 ± 72.61	3.45	**0.032**
PDW	12.97 ± 2.32	12.85 ± 2.47	12.64 ± 2.50	1.29	0.277
MPV	10.80 ± 1.35	10.72 ± 1.38	10.54 ± 1.50	2.29	0.102
WBCs	7.88 ± 2.28	4.82 ± 0.56	4.93 ± 0.46	461.01	**< 0.0000001**
RBCs	4.83 ± 0.46	7.39 ± 2.03	8.03 ± 2.19	351.11	**< 0.0000001**

One-way ANOVA. PLT: Platelet counts (K/μL). PDW: Platelet distribution width (fL). MPV: Mean platelet volume (K/μL). WBCs: White blood cells. RBCs: Red blood cells. Values in bold are significant.

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Table 2. Comparison of the medication groups in the bipolar disorder group.

	Lithium group (n = 124)	Valproate group (n = 203)	Mood stabilizer free group (n = 51)	F	P
MPV	10.72 ± 0.86	10.98 ± 1.29	10.27 ± 2.25	6.10	0.003
PDW	12.78 ± 1.90	13.30 ± 2.34	12.19 ± 2.95	5.44	0.005
PC	268.15 ± 65.34	230.96 ± 62.95	256.27 ± 72.37	13.24	< 0.001
WBCs	8.55 ± 2.52	7.46 ± 1.93	7.76 ± 2.59	9.16	< 0.001
RBCs	4.93 ± 0.49	4.79 ± 0.44	4.75 ± 0.40	4.70	0.010

One-way ANOVA. PDW: Platelet distribution width. MPV: Mean platelet volume. PC: Platelet counts. WBCs: White blood cell counts. RBCs: Red blood cell counts. MPV and WBC values were not homogeneous variants and therefore we used the Tamhane post hoc test. Other variables were compared using the Bonferroni test.

than in Li-treated patients (P = 0.017), and lower in mood stabilizer-free patients than in Li-treated patients (P = 0.041)). MPV did not differ between the groups in post hoc comparisons. Furthermore, we found a correlation between serum Li levels (mean = 0.61 ± 0.53 mmol/L) and WBCs (P = 0.044, rho = 0.18). One of the several limitations in this analysis was that all patient groups were on various treatments, including antipsychotics and antidepressants. Another limitation was that we could not collect information regarding comorbid medical conditions or substance use statuses. In addition, the groups were not homogeneous and there was no healthy control group.

Lower platelet counts in the bipolar disorder in comparison with the depressive disorder group could be related to the lower platelet numbers in the VPA group. These results are consistent with previous studies and show that Li stimulates all progenitor blood cell lines in bone marrow, whereas VPA influences platelet count and function. The distinct effects of VPA and Li may reduce the possibility of involvement of similar mechanisms of action such as inhibition of glycogen synthase kinase-3. The linear relationship between serum Li levels and WBC may imply a dose-dependent stimulation of bone marrow. The differential effects of Li and VPA on blood cells could be valuable in detecting their molecular targets and growth factors in future studies.

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