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Original Research Article

Efficacy and Adverse Effect Profile of Lithium versus Divalproex Sodium in the Treatment of Patients with Bipolar Affective Disorders on Combination Therapy: A Comparative, Naturalistic, Clinical Study

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Conflict of interest: Nil

Abstract:

Background: Bipolar disorder is a complicated psychological disorder that affects patients on an individual and social level. The purpose of this study is to evaluate the effectiveness of lithium and divalproex sodium in treating patients with bipolar illness who are receiving combination therapy.

Methods: The effectiveness of lithium and divalproex sodium in the treatment of bipolar disorder was compared in a prospective, comparative trial. The study included patients with bipolar disorder of either sex who were between the ages of 18 to 65. The YMRS scale was used to analyze efficacy at baseline and four weeks later.

Results: The study included 68 bipolar disorder patients who were experiencing manic episodes at the time of the trial. Two groups were formed out of them. One group took lithium, and the other group took divalproex sodium. The medications that were given to both groups at the same time were similar. There were eighteen female patients and fifty male patients. At baseline and at the conclusion of four weeks, YMRS scoring was completed. The baseline and 4-week YMRS scores for the Divalproate sodium group were 31.22 and 29.13, respectively. The baseline and 4-week YMRS scores for the lithium group were 30.88 and 28.93, respectively. The YMRS scores in both groups significantly decreased over the course of four weeks, with a p-value of less than 0.05. Nevertheless, there was no statistically significant difference between the two groups' YMRS scores after four weeks. Both groups experienced the same level of efficacy.

Conclusion: After four weeks of medication, lithium and divalproate sodium were equally effective in treating bipolar illness. By the end of four weeks, patients had significantly improved with both medications.

Keywords: lithium, divalproex sodium.

Introduction

Bipolar disorder is a complicated mental illness that affects people on an individual and social level. Complex pharmaceutical treatment is necessary. [1] Mood swings from euphoria to sadness are hallmarks of bipolar disorder. Social and familial relationships may be severely disrupted by this illness. According to a UK study, the mortality rate for bipolar illness patients was greater than the overall population one year after they were discharged from the hospital. [2] Bipolar disorder has been more common in recent years, which necessitates further research in this field. Lithium and divalproex sodium are currently the first-line medications used to treat bipolar disorders. To manage agitation, excessive activity, and psychotic symptoms, a second-generation atypical antipsychotic medication is frequently given in clinical practice. The first medication to be found to be effective in treating bipolar disorder was lithium. For more than 60 years, it has been in use. In both acute phase sickness and maintenance treatment, it remains the primary mood stabilizer.

However, different medications are being employed because of the sluggish start of effect and frequent requirement for therapeutic drug monitoring. Divalproex sodium, an antiepileptic medication, is one example. The purpose of this study is to evaluate the effectiveness of lithium and divalproex sodium in treating individuals with bipolar affective disorder who are receiving combination therapy.

Material and Methods

This study was comparative, prospective and hospital based from March 2024 to October of 2024 and it was carried out at the Department of Pharmacology with Department of Psychiatry in Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar. This sample has a size of 68. For each patient involved in the trial, a signed informed agreement was obtained. Bipolar Affective Disorder patients with current episodes of mania or hypomania who were admitted to the inpatient ward and were of either sex and between the ages of 18 to65 were included in the study. Participants in the study were not allowed to have serious co-occurring mental or medical disorders. An initial sample of thirty-six bipolar disorder patients on Divalproex sodium and thirty-two bipolar disorder patients taking lithium were included. A brief history and examination were carried out in each patient. The data was entered in a proforma sheet. The investigations carried out were noted. YMRS scoring was done at baseline. The patients were followed up for a period of 4 weeks. The YMRS scoring was done again at the end of 4 weeks. Adverse drug events, if any were recorded. The collected data was analysed using Mean, Frequency, Percentage, Standard Deviation, paired and unpaired t test, chi-square test.

Results

The age distribution for the sample size is shown in Figure 1. The sample size distribution by gender is depicted in Figure 2. Males make up the majority of the study's participants. The age at which bipolar disorder first manifests itself is displayed in Table 1. The age range of 31 to 40 years old had the highest number of patients. The distribution of the study sample according to the first episode's Polarity is displayed in Table 2. Mania predominated in the initial episode that was diagnosed. The entire length of the sickness is displayed in Table 3. The groups' YMRS scores are displayed in Table 4, and the paired sample test is displayed in Table 5. At baseline and at the conclusion of the four weeks, YMRS scoring was completed. In the Divalproate sodium group the YMRS scores at baseline at 4 weeks were 31.22 and 29.13 respectively. In the Lithium group the YMRS scores at baseline at 4 weeks were 30.88 and 28.93 respectively. Both the groups had a significant reduction in the YMRS scores in 4weeks with a p value of less than 0.05. However when the YMRS scores were compared between the two groups at the end of 4 weeks there was no statistical difference. The efficacy was same in both the groups.

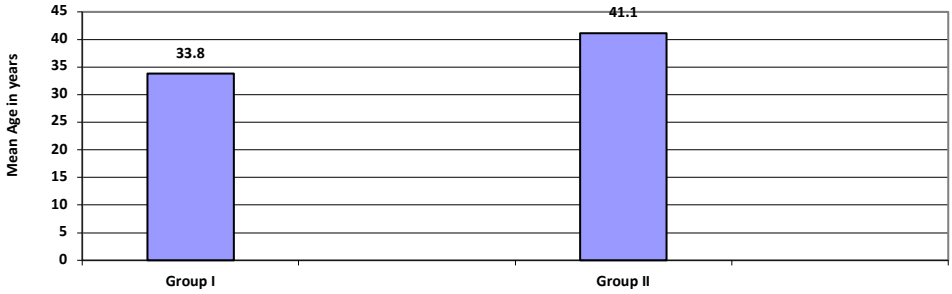

Figure 1: Graph showing the age distribution

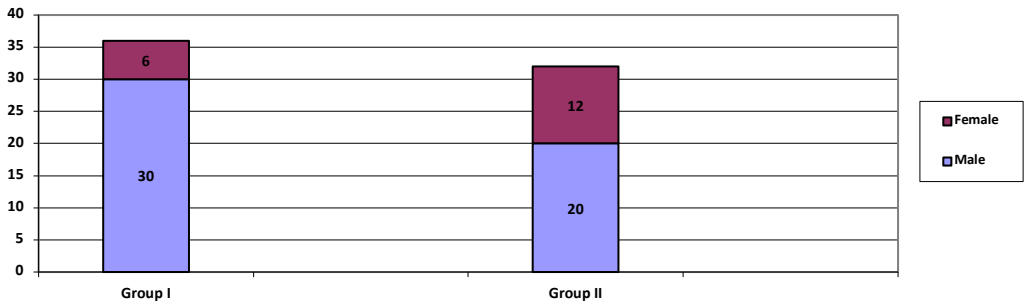

Figure 2: Graph showing the distribution of the study sample according to gender

Table 1: Table showing the age of first onset of Bipolar Disorder value

Age of first onset	Group I	Group II	Total
11-17 No. (%)	6(16.7%)	8(25.0%)	14(20.6%)
18-30 No. (%)	20(55.6%)	3(9.4%)	23(33.8%)
31-40 No. (%)	6(16.7%)	10(31.3%)	16(23.5%)
41-50 No. (%)	4(11.1%)	7(21.9%)	11(16.2%)
51-64 No. (%)	0(0.0%)	4(12.5%)	4(5.9%)
Total No. (%)	36(100.0%)	32(100.0%)	68(100.0%)

Table 2: Table showing the distribution of the study sample based on Polarity of the first episode

	Group I	Group II	Total
D No. (%)	2(5.6%)	1(3.1%)	3(4.4%)
M No. (%)	34(94.4%)	31(96.9%)	65(95.6%)
Total No. (%)	36(100.0%)	32(100.0%)	68(100.0%)

P-value = 0.626

Table 3: Table showing the total duration of the illness

Total Duration	Group I	Group II	Total
<1 No. (%)	8(22.2%)	6(18.8%)	14(20.6%)
1-5 No. (%)	12(33.3%)	4(12.5%)	16(23.5%)
5-10 No. (%)	7(19.4%)	14(43.8%)	21(30.9%)
10-20 No. (%)	7(19.4%)	7(21.9%)	14(20.6%)
>20 No. (%)	2(5.6%)	1(3.1%)	3(4.4%)
Total	36(100.0%)	32(100.0%)	68(100.0%)

p-value = 0.150

Table 4: Table showing the YMRS scores between the two groups

	Group	N	Mean	Std. Deviation	t-value
YMRS	Group I	36	31.22	3.735	0.403
	Group II	32	30.88	3.329	P=0.689ns
YMRS (4)	Group I	32	29.13	3.949	0.210
	Group II	30	28.93	3.172	P=0.835ns

Table 5: Table showing the Paired Samples Test

	Group	Mean	Std. Deviation	t-value	p-value
Group I	YMRS-YMRS(4)	2.531	1.831	7.819	0.000
Group II	YMRS-YMRS(4)	1.967	2.076	5.189	0.000

Discussion

Bipolar depression is extremely difficult to treat. If the right diagnosis is obtained and treatment is started as soon as possible, it can be successful. The effectiveness of lithium and divalproex sodium in treating bipolar disorder was assessed and contrasted in this study. 68 patients in all, split into two groups, took part of the study. Of the 36 patients in the Divalproex Sodium group, four were lost to follow-up. Of the 32 patients included in the lithium, two were lost to follow-up. Thus, 62 patients in all were available for assessment. The average age of the patients in this trial was 41.1 years for the lithium group and 33.8 years for the divalproate sodium group. A related study comparing the effectiveness of lithium and divalproate sodium in the treatment of bipolar disorder was conducted by Kessing LV et al. In that study, the average age of the patients in the lithium group was 49 years old, whereas the average age of the patients in the divalproate group was 52 years old. [1] A total of 73.5% of the patients in this study were males, and 26.5% were females. There were 42% males and 58% females in the Kessing LV et al. study.[1] Nonetheless, the majority of research indicates that the frequency of bipolar disorder is almost equal among males and females.(4) According to this study, the illness is more common in those between the ages of 18 and 30, accounting for 33.8% of the sample population.

The age group of 31–40 years old comes next, accounting for 23.5% of the study population. The age group of 51–64 years old had the fewest patients, accounting for 5.9% of the total population. According to a study by Kessing LV et al., the condition often manifests at age 21. [1] Mania was the initial episode of bipolar disorder in the majority of the patients. Mania was the initial episode of bipolar disorder in 65 out of 68 cases. Mania is the initial sign of bipolar disorder,

according to Sadock BJ.[5] A total of 30.9% of the study population fell into this time frame, with the majority of patients in this study having had their illnesses for five to ten years. With a p-value of 0.150, the overall length of the illness was similar for the two groups. After four weeks of treatment, this study found that the YMRS scores for the lithium and divalproate groups were statistically significantly. Nonetheless, there was no statistically significant difference in the effectiveness of the two groups. As a result, after four weeks, both medications were equally effective. In order to compare the efficacy of divalproex sodium with that of lithium and a placebo in individuals suffering from acute mania, Bowden CL et al. conducted a randomized, double-blind, parallel-group research. According to the study's findings, divalproex sodium and lithium both considerably reduced acute manic symptoms more effectively than a placebo.[6] A study comparing the effectiveness of valproate and lithium carbonate in treating acute mania was conducted by Freeman TW et al. [7].

According to the study findings, both valproate and lithium were useful in reducing manic symptoms, with lithium being marginally more helpful overall. A lower need for intervention initiation for an emergent mood episode was seen in the BALANCE study, which compared valproate monotherapy with lithium monotherapy in the treatment of bipolar disorder.[8] Kessing LV et al. conducted a population-based, nationwide register linkage study with a 12-year follow-up duration. Of the 4268 subjects, 719 were given valproate and 3549 were given lithium after being diagnosed with bipolar disorder. Compared to lithium, valproate increased the rate of switch/add-on to the opposite medication (valproate or lithium), antidepressants, antipsychotics, or anticonvulsants (other than valproate). Compared to lithium, the rate of psychiatric hospital admissions was higher for valproate. According to the study's findings, lithium medication was generally better than valproate treatment. One Divalproate sodium is more beneficial in patients with co-morbid disorders, while lithium is effective in those with typical manic episodes.[5] This was supported by the current study, which found that divalproate sodium was the recommended treatment for bipolar disorder with co-morbid disorders.

Conclusion

Bipolar disorder treatment is difficult. The secret to successfully managing people with bipolar disorder is early identification and therapy. After four weeks of medication, the current study found that lithium and divalproate sodium were equally effective in treating bipolar disorder patients with current episode mania. By the end of four weeks, patients had significantly improved with both medications. The two medications were both well tolerated. To re-emphasize this study, however, larger investigations with a larger sample size and longer follow-up periods are needed.

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