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Original Research Article

Comparison of safety and efficacy of lithium and lithium with SSRI in bipolar disorder

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ABSTRACT

Background: Bipolar disorder is a serious psychiatric illness resulting in depression and mania that affects approximately 1.5% of the world population and represents a significant source of individual morbidity and mortality. Hence the present study was undertaken to compare the safety and efficacy of Lithium and Lithium with SSRI in Bipolar disorder.
Methods: Study was conducted in outpatient department, Department of Psychiatry, Basaveshwar Teaching and General Hospital attached to Mahadevappa Rampure Medical College, Kalaburagi, Karnataka. After obtaining Informed and written consent, Total 60 patients were selected after inclusion and exclusion criteria. Patients were diagnosed according to MINI and were divided into 2 groups, Group 1: Patients receiving Lithium 800-1200 group 2: Patients receiving Lithium + Escitalopram 20 mg/those intolerants to Escitalopram were given Sertraline 100 mg. Both groups were followed up regularly at interval of 1, 3, 5 and 8 weeks
Results: Findings were tabulated according to comparative tools like MADRS, YMRS, C-SSRS, CGI- BP & QOLS, they were subjected to t-test and ANOVA to verify the outcome
Conclusions: Patients treated with Lithium + SSRI showed to have better quality of life and had a lower risk of switch to manic episodes.

Keywords: Antidepressant, Mood disorder, Montgomery–Åsberg depression rating scale, Quality of life scale

INTRODUCTION

Bipolar disorder is a long-term, mental illness characterized by depression and mania which involves instability of mood and energy. It is associated with high rates of suicidal incidence and medical comorbidities.[1] In the year 1949, John Cade introduced Lithium which continues to be the best modality of treatment of BPD.[2] Lithium produces changes in sodium transport within nerve and muscle cells and influences the metabolism of neurotransmitters; particularly catecholamines and serotonin. Lithium may alter intracellular signalling via second messenger systems by inhibiting inositol monophosphate. This inhibitory action blocks neurotransmission mediated by the phosphatidylinositol secondary messenger system.[3] Manic phase of bipolar disorder generally responded well to Lithium; however, the efficacy of Lithium in depressive phase was mixed. The commonly used medications like Selective serotonin reuptake inhibitor (SSRI) and Selective Norepinephrine reuptake inhibitor (SNRI) which have greater efficacy in depressive phase of bipolar disorder.[4] A cautious approach to antidepressant uses in bipolar disorder is strongly recommended by the American Psychiatric Association guidelines.[5] The available studies fail to provide evidence of use of alone antidepressant prevention of depressive relapse. Moreover, there is likely a significant more mood episode over time and possible rapid cycling with long term use of antidepressant in bipolar disorder. The other

issue is the long-term risk of antidepressant induced mood destabilization.[6] Hence the present study is being taken up.

METHODS

Study place

This study was carried out in Department of Psychiatry, Basaveshwar Teaching and General Hospital, attached to Mahadevappa Rampure Medical College, Kalaburagi.

Study duration

The study period was of 8 weeks from September 2014 to October 2015.

Inclusion criteria

Patients included in the study diagnosed with Bipolar disorder I/II currently in depression according to DSM V TR criteria of either sex in age group of 18-60 years.[7]

Exclusion criteria

Patients excluded in the study with Current axis I primary psychiatric disorder diagnosis other than bipolar disorder, requiring admission/ECT, with mixed episodes, with psychosis/ substance abuse, with chronic physical illness (neurological illness, CVA, head injury) organic mental disorder or active medical condition that could confound diagnosis or clinical characterization of psychopathology and with thyroid disorder.

Informed consent:

Informed and written consent was taken from all the patients in their own vernacular language.

Ethical approval

Ethical committee approval was obtained from Institutional Ethics Committee, M.R.Medical College, Kalaburagi. Protocol No:181106 dated 30/11/2018, prior to the commencement of the study.

Study method

Total 60 patients were included in the study after inclusion and exclusion criteria and two groups of 30 patients each were enrolled.

Grouping

Group 1 patients receiving only Lithium (30 Patients) (Lithium group). Group 2 patients receiving Lithium with SSRI (30 Patients) (Lithium with SSRI group). Patients diagnosed using mini-international neuropsychiatry inventory (MINI) were included; Objective depressive symptoms were assessed by MADRS Manic symptoms were assessed by YMRS.[8-10] Consecutive patients were allotted to one of the two groups. One group received Lithium only while the other group received Lithium with SSRI. Patients were followed up for 8 weeks. There were visits at 1st, 3rd, 5th and 8th week.

Maximum dose of Lithium was 800-1200 mg, Maximum dose of SSRI Escitalopram was 20 mg and patients who did not tolerate Escitalopram received Sertraline to a maximum dose of 100 mg.The drugs were procured from the local market. Following Scales were used in the study.

Mini international neuropsychiatry inventory (MINI) is a short structured clinical interview used here to confirm the diagnosis and detect any comorbid conditions. Montgomery asberg depression rating scale (MADRS) is a ten-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorder. Young mania rating scale (YMRS) is used to assess manic symptoms Columbia suicide severity rating scale (C-SSRS) is a suicidal ideation rating scale which identifies behaviors indicative of individuals intent to commit suicide.[11]

Clinical Global Impression Scale for Bipolar Disorder (CGI-BP) is used to rate the severity of manic and depressive episodes and the degree of change from immediately preceding phase and from worst phase of illness. Scale comprises of 3 Parameters.[12] severity of illness, global improvement, efficacy index

The QOLS is a valid instrument for measuring quality of life across patient groups and cultures and is conceptually distinct from health status or other causal indicators of quality of life.[13]

Statistical analysis

Complete data was analyzed using SPSS software version 20.0, t-test and ANOVA were used to assess the significance of difference of mean between 2 or more groups respectively. All p-values were two tailed and statistical significance was set up at $p<0.05$.

RESULTS

The mean age of patient in group 1 was 33.30 (SD ±9.59 years) whereas group 2 was 32.80 (SD ±7.98 years). In Group 1 males constituted 63 % and female were 37 %. In group 2 males constituted 43 % whereas 57% were females. Majorities were graduates and married in both groups. All patients are belonging to nuclear family (Table 1).

The mean MADRS score at the start of study was 26.967 (±0.858) in group 1 and 26.700 (±0.782) in group 2 and at the end of 8th week, Lithium+SSRI is 11.300 and Lithium alone is 12.400 which infers there is improvement in the bipolar disorder with Lithium+SSRI group (Table 2). The mean YMRS score at the start of the study was 0.533

(±0.213) in group 1 and 0.400 (±0.195) in group 2 and at the end of 8th week, Lithium+SSRI is 0.400 and Lithium alone is 0.067 which infers there is improvement in the bipolar disorder with Lithium+SSRI group (Table 3). The mean CGI-BP I score at the start of the study was 4.200 (±0.080) in group 1 and 4.100 (±0.056) in group 2 and at the end of 8th week, Lithium+SSRI is 2.500 and Lithium alone is 2.40 which shows there is improvement in the severity of illness in bipolar disorder with Lithium+SSRI group (Table 4A). The mean CGI-BP II score at the start of the study was 4.000 (±0.000) in group 1 and 4.000 (± 0.000) in group 2 and at the end of 8th week, Lithium+SSRI is 1.533 and Lithium alone is 1.767 which shows there is improvement in the bipolar disorder with Lithium+SSRI group (Table 4B). The mean CGI-BP III score at the start of the study was 4.000 (±0.000) in group 1 and 4.000 (±0.000) in group 2 and at the end of 8th week, Lithium+SSRI is 1.533 and Lithium alone is 1.767 which shows there is improvement in the efficacy index in bipolar disorder with Lithium+SSRI group (Table 4C). The mean QOL score at the start of study was 60.167 (±2.122) in group 1 and 68.567 (±1.475) in group 2 and at the end of 8th week, Lithium+SSRI is 99.333 and Lithium alone is 91.633 which shows improvement in the quality of life in the bipolar disorder with Lithium+SSRI group (Table 5).

Table 1: Socio demographic profile.

		Group N (%)		
		Lithium n=30	**Lithium+SSRI (n=30)**	**P value**
Age (in years)		33.30±9.59	32.80±7.98	0.827
Sex	Male	19 (63.33)	13 (43.33)	
	Female	11 (36.66)	17 (56.66)	
Education	Illiterate	1 (3.33)	0 (0)	0.770
	Primary	1 (3.33)	3 (10.0)	
	Secondary	5 (16.66)	1 (3.33)	
	Graduate	20 (66.66)	23 (76.66)	
	Post graduate	3 (10.0)	3 (10.0)	
Marital status	Single	6 (20.0)	7 (23.33)	0.770
	Married	23 (76.66)	22 (73.33)	
	Divorced	1 (3.33)	0 (0)	
	Widowed	0 (0)	1 (3.33)	
Occupation	Unemployed	1 (3.33)	1 (3.33)	0.107
	Student	4 (13.33)	6 (20.0)	
	Housewife	9 (30.0)	11 (36.66)	
	Service	7 (23.33)	10 (33.33)	
	Unskilled worker	0 (0)	1 (3.33)	
	Business	3 (10.0)	1 (3.33)	
	Self employed	6 (20.0)	0 (0)	

Values are expressed as mean±SD. P value<0.05 is considered significant.

Table 2: MADRS score.

Weeks	Lithium only	Lithium+SSRI	P value
0	26.967±0.858	26.700±0.782	0.819
1	24.500±0.856	24.500±0.733	1.000
3	21.367±0.804	20.267±0.671	0.298
5	17.667±0.800	16.433±0.802	0.223
8	12.400±0.924	11.300±0.642	0.332
Overall	20.580	19.840	

Values are expressed as mean±SD. P value<0.05 is considered significant.

Table 3: YMRS score.

Weeks	Lithium only	Lithium+SSRI	P value
0	0.533±0.213	0.400±0.195	0.646
1	0.233±0.133	0.333±0.168	0.643
3	0.100±0.100	0.133±0.133	0.507
5	0.067±0.067	0.200±0.111	0.656

Continued.

Weeks	Lithium only	Lithium+SSRI	P value
8	0.067±0.067	0.400±0.400	0.414
	0.200	0.293	

Values are expressed as mean±SD. P value<0.05 is considered significant.

Table 4A: CGI-BP I (Severity of illness scale).

Weeks	Lithium	Lithium+SSRI	P value
0	4.200±0.080	4.100±0.056	0.343
1	4.100±0.111	3.933±0.082	0.232
3	3.533±0.104	3.500±0.093	0.812
5	3.233±0.092	3.100±0.056	0.220
8	2.400±0.141	2.500±0.093	0.555
	3.493	3.427	

Values are expressed as mean±SD. P value<0.05 is considered significant.

Table 4B: CGI-BP II (Global improvement).

Weeks	Lithium	Lithium+SSRI	P value
0	4.000±0.000	4.000±0.000	1
1	3.067±0.067	3.067±0.046	1
3	2.600±0.091	2.533±0.093	0.610
5	2.233±0.079	2.067±0.046	0.073
8	1.767±0.092	1.533±0.093	0.079
	2.7330	2.640	

Values are expressed as mean±SD. P value<0.05 is considered significant.

Table 4C: CGI-BP III (Efficacy index).

Week	Lithium	Lithium+SSRI	P value
0	4.000±0.000	4.000±0.000	1
1	3.067±0.067	3.067±0.046	1
3	2.600±0.091	2.533±0.093	0.610
5	2.233±0.079	2.067±0.046	0.073
8	1.767±0.092	1.533±0.093	0.079
	2.7330	2.640	

Values are expressed as mean±SD. P value<0.05 is considered significant.

Table 5: QOL score.

Week	Lithium only	Lithium+SSRI	P value
0	60.167±2.122	68.567±1.475	0.002*
1	66.700±2.211	74.500±1.371	0.004*
3	73.433±1.832	82.600±1.159	0.000*
5	80.300±1.798	90.400±1.099	0.000*
8	91.633±1.847	99.333±0.796	0.000*
	74.447	83.080	

Values are expressed as mean±SD. P value<0.05 is considered significant, Significant p value*

DISCUSSION

The sociodemographic profile of the patient is in Table 1. The mean age (in years) of Group 1 was 33.30±9.59 and for group 2 was 32.80±7.98 which was not statistically significant. Males constituted about 63% in group 1 and 43 % for Group 2 with no statistically significant difference. Majority were graduates across both group and Majority were married in both groups. There were no statistically significant differences between the two groups across sociodemographic parameter. MADRS score in group 1 was 26.967±0.858 and in group 2 was 26.700±0.782. MADRS score was less in consecutive visits as compared

to previous visits in each group but between groups there was no statistically significant difference. This is almost similar to the finding reported by Sach et al.[14] STEP BD study in 2007, Young et al.[15] YMRS score in group 1 was 0.533±0.213 and in group 2 was 0.400±0.195. Overall, the risk of switch in both groups was similar and was not statistically significant. C-SSRS score was 0 in both the groups all throughout the study. There was also no increased risk of suicidal ideation in both groups assessed by C-SSRS. QOL score in group 1 was 60.167±2.122 and in group 2 was 68.567±1.475.QOL score was more in the group 2; this was maintained during each visit. The higher score indicates higher quality of life in group 2.CGI-BP score in group 1 was 4.200±0.080 and in group 2 was 4.100±0.056. There was no statistically significant difference between the two groups in any of the above-mentioned clinical parameters. The patients were assessed at an interval of week 1, 3, 5 and 8.

The sample size was relatively small, thus limiting conclusions in general and especially from sub group analyses. The lack of statistical power for some analyses warrants a further study with a larger sample. Study had short duration of follow up of only 2 months, hence long-term consequences/safety of prolonged antidepressant use could not be assessed.

Strengths of the study were usage of standardized research diagnostic criteria. Usage of standardized rating scales for the assessment. Both the group being comparable for socio-demographic profile.

CONCLUSION

It can be inferred that addition of antidepressant like SSRI to Lithium in the treatment of Bipolar depression improved the quality of life. Overall, the risk of switch in mood in the both the groups was similar and was not statistically significant. Antidepressant use was not associated with increased risk of mania. There was no increased risk of suicidal ideation in both groups. There was no statistical difference in clinical global impression scale for bipolar disorder used to rate the severity of manic and depressive episodes and the degree of change from immediately preceding phase and from worst phase of illness in both groups.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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