

LITHIUM TREATMENT IN AFFECTIVE DISORDERS

A. K. TANDON¹, M. D.
RAM ASARE², M. B., B.S.
V. C. SAXENA³, M.D.

SUMMARY

50 manic patients of unipolar and bipolar affective illness were placed on oral lithium 600-1500 mg daily and serum levels in the range of 0.49-1.23 mEq/L. A better response in bipolar disorders than unipolar was observed. Besides, a much better response to lithium therapy is observed in patients with disease of longer duration and a positive history of affective illness in blood relations. Therapeutic effect had no relationship in terms of age or sex of the patients.

The western medical literature is replete with studies related to role of lithium in affective disorders (Davis, 1967 ; Fieve *et al.*, 1976). On the contrary studies on lithium in Indian subjects are still not so common. In recent years many workers have explored different aspects of lithium treatment (Ghosh *et al.*, 1977 ; Narayanan *et al.*, 1977 ; Venkoba Rao and Harihara subramanium, 1978, Prakash *et al.*, 1978). However, the subject is still unexplored in many aspects and gives profound scope of research.

Several factors influence response to lithium. These include pharmacokinetic factors relating to dose and serum concentration, its absorption and excretion and the clinical variables like age, sex, nature of illness, total duration of illness and a family history (Ananth, 1977). The present study is aimed to evaluate efficacy of lithium in relation to the above factors.

MATERIAL AND METHODS

The sample of this study was obtained from patients attending the Psychiatric unit of S. R. N. Hospital Allahabad, during February 1979 to January 1980. A total number of 50 patients suffering from affective illness (Unipolar and Bipolar) formed the material. Of these 50, 23 were hospital-

ized and the rest were attending Psychiatric OPD. Their ages ranged between 16 and 65 years.

After the initial diagnosis of affective psychosis, the cases were subjected to a detailed history, physical examination and a battery of investigations to exclude any evidence of cardiac or renal disease. Presence of renal or cardiac illness, pregnancy and lactation have been taken as contraindications to lithium therapy. Investigations included : Urine examination, Blood urea, Blood sugar and Electrocardiogram. Psychometric assessment was done on a 24 point Hamilton Rating Scale for depression (1960) and 17 point Beigel's Rating Scale for mania (Beigel *et al.*, 1971). Rating on these scales was repeated on subsequent follow up visits to assess the improvement.

All the patients were started on lithium Carbonate 500-750 mg per day after blood samples for haemogram (Hb. TLC, DLC). Two days after the commencement of lithium then on weekly and later at longer intervals serum lithium was estimated by flame photometry using Amdisen's method (Amdisen, 1967). The blood sample for serum lithium estimation were drawn twelve hours after the last dose of lithium. The dose was increased by 150-250 mg every 2nd or 3rd day till the desired effect was

¹Lecturer in Psychiatry. }

²Postgraduate student }

³Reader in Pharmacology, J }

M.L.N. Medical College, Allahabad, U. P.

obtained and without any observable side effects. Serum lithium level was maintained at a level below the 1.6m Eq/L. The maintenance dose ranged between 600-900 mgm per day.

RESULTS

The present sample consists of 50 patients of affective illness on lithium treatment, which included 24 cases of mania, 18 cases of depression and 8 cases of MDP. 50% of the cases had been ill for the past 1-5 years, 36% for more than 6 years and the rest 14% reported that their illness was of less than a year's duration.

Table 1 shows mean serum lithium concentration at different oral doses. In the majority of subjects lithium was given in dosage of 600 to 1200 mg daily. At maximum dose of 1500 mg/day the mean lithium concentration was 1.23 mEq/L.

Pre-treatment psychometric assessment for manic states shows mean manic score of 19.60 and 14.36 for unipolar and bipolar respectively. After treatment with lithium the mean score was observed below 2. Similarly a marked reduction of depressive score was noticed in depressive patients after the lithium therapy (Table II). A higher percentage reduction in manic scores was observed than in depression. A maxi-

TABLE I—*Oral odse and Serum Lithium Concentration*

Dose of Lithium (in mgm)	Serum Lithium concentration (Mean) mEq/L	No. of values	Range
450	0.32±0.06	5	0.25—0.4
500	0.40±0.06	6	0.30—0.46
600	0.49±0.04	14	0.40—0.54
750	0.73±0.08	18	0.54—0.82
900	0.78±0.09	17	0.58—0.94
1000	0.93±0.07	21	0.77—1.06
1050	0.94±0.09	34	0.75—1.14
1200	1.07±0.08	22	0.95—1.20
1250	1.07±0.93	14	0.90—1.24
1350	1.15±0.85	11	0.96—1.28
1500	1.23±0.087	7	1.12—1.34
Total	0.32—1.23	179	0.25—1.34

mum reduction of mean scores was found in the manic phase of bipolar illness (93.0%).

The response to lithium was assessed on the basis of percentage reduction in total scores after one month of treatment with the drug. On the basis of response demonstrated by these subjects they were categorised into the following three groups—*Group I*—(Good responders)

Reduction in score was more than 90%.

TABLE II—*Mean values of scores of Hamilton rating scale (depression) and Beigel's rating scale (mania)*

	Pretreatment Phase	Number of days after lithium treatment				% reduction (mean) of score at 30 days from pre-treatment phase
		7 days	14 days	30 days	more than 1 month	
<i>Unipolar :</i>						
Mania (N=24)	19.6±4.3	12.0±2.7	5.9±3.10	3.20±2.2	1.7±1.6	83.5
Depression (N=18)	26.8±9.6	18.7±6.5	13.3±5.2	9.30±6.1	3.6±1.8	65.2
<i>Bipolar</i>						
Manic Phase (N=4)	14.3±2.6	9.3±1.7	3.8±1.7	1.0±0.7	1.0±0.7	93.0
Depressive (N=4)	25.5±4.2	13.8±2.9	11.5±3.9	6.2±2.5	4.7±1.0	75.5

Group II—(Moderate responders)

Reduction in score was 70 to 90%.

Group III—(Poor responders)

Reduction was less than 70% or those who did not respond at all.

Rating of the subjects in terms of their response revealed that 26% of the sample could be labelled as good responders, 52% as moderate responders and 22% poor responders. A better response was observed in patients with longer duration of illness. All the cases who were suffering from the illness for more than 6 years duration responded except one. The analysis of response in relation to family history showed a higher incidence of good responders in patients with a similar psychiatric illness in blood relations (Table III).

TABLE III—Response to lithium in relation to different factors

Sl. No.	Variables	Response					
		Gr. I (GR)		Gr. II (MR)		Gr. III (PR)	
		N	%	N	%	N	%
1.	<i>Type of affective illness</i>						
	Mania (N=24)	9	37.5	12	50.0	3	12.5
	Depression (N=18)	2	11.1	8	44.4	8	44.4
	M.D.P. (N=8)	2	25.0	6	75.0
2.	<i>Sex</i>						
	Male (N=44)	11	25.0	22	50.0	11	25.0
	Female (N=6)	2	33.3	4	66.7
3.	<i>Duration of illness (in yrs.)</i>						
	Less than 1 (N=7)	1	14.3	3	42.8	3	42.8
	1 to 5 (N=25)	3	12.0	15	60.0	7	28.0
	6 to 10 (N=7)	4	57.1	2	28.6	1	14.3
	More than 10 (N=11)	5	45.5	6	54.5
5.	<i>History of Psychiatric illness in blood Relations</i>						
	Present (N=20)	7	35.0	11	55.0	2	10.0
	Absent (N=30)	6	20.0	15	50.0	9	30.0

DISCUSSION

In the present series, 50 patients of unipolar and bipolar affective illness, 44 males and 6 females were placed on oral lithium in a dose of 600-1500 mg daily after proper psychometric assessment on respective scales for mania and depression. Regulation of lithium dosage was done by monitoring its concentration in the blood at regular intervals and careful observation for appearance of serious side effects.

Majority of the patients (94%) showed significant improvement. Only three patients who were suffering from recurrent depression did not show any response and one relapsed after stopping the medication. The incidence of non-responders (6%) is comparable to Misra and Burns (1977) and Prakash *et al.* (1978), who observed non responders as 8.4% and 9.09% respectively in their reports. The dose of the lithium required to achieve remission in our patients was lesser in comparison to western countries. In other words effective serum concentration (0.6—1.2 mEq/L.) was achieved with lesser amounts of lithium carbonate (750—1500 mg/day) than that required in western population (900—1800 mg/day), suggesting thereby a racial factor.

In the light of observations of the present study lithium can be said to have better therapeutic effect in bipolar than unipolar illness and amongst unipolar, in manics than depressives. Positive correlation of response in relation to type of affective illness coincides with reports of other workers (Gershon and Yuwiler, 1960, Venkoba Rao and Hariharasubramaniam, 1978). A better beneficial effect was a feature in patients, who had a history of affective illness in blood relations (35% v.s. 20%). Several investigators (Mendelwicz *et al.*, 1972; Prien *et al.*, 1972 and Ghosh *et al.*, 1977) have also reported a positive correlation between response and presence of affective illness in first degree relatives.

The present study revealed a higher incidence of good responders with increasing duration of illness. None of the patients, with a duration of more than 10 years, illness failed to respond with this treatment. Venkoba Rao and Hariharasubramaniam (1978) also observed a similar finding but Schou *et al.* (1967) reported that there was no association between response and duration of illness.

REFERENCES

- AMDISEN, A. (1967). Serum Lithium determination for clinical use. *Scandinavian Journal of clinical and laboratory investigation*, 20, 104.
- ANANTH, J. V. (1977). Prediction of lithium response : Clinical variables. *Indian J. Psychiat.* 19, 20.
- BEIGEL, A., MURPHY, D. I. and BUNNEY, W. E. Jr. (1971). The manic state rating scale. *Arch. Gen. Psychiat.*, 25, 256.
- DAVIS, J. M. (1967). Overview : Maintenance therapy in Psychiatry II. *Affective disorders. Am. J. Psychiat.*, 133, 1.
- FIEVE, R. R., KUMBARACI, T. and DUNNER, D. L. (1976). Lithium prophylaxis of depression in bipolar I, bipolar II and Unipolar patients. *Am. J. Psychiat.*, 133, 925.
- GERSHON, S. and YUWILLER, A. (1960). Lithium ion : a specific approach to the treatment of mania. *J Neuropsychiat.*, 1, 229.
- GHOSH, A., WIG, N. N. and SRINIVASA MURTHY, R. (1977). Prophylactic value of lithium in manic depressive psychosis—Genetic aspects. *Ind. J. Psychiat.*, 19, 73.
- MENDELWICZ, L. FIEVE, R. R., STALLONE, F. and FLEISS, I. L. (1972). Genetic history as a predictor of lithium response in manic-depressive illness. *Lancet*, 1, 599.
- MISRA, P. C. and BURNS, B. H. (1977). Lithium non-responders in a lithium clinic. *Acta. Psychiat. Scand.*, 55, 32.
- NARAYANAN, H. S. and RAO, B. B. S., MALLIKARJUNIAH. (1977). A clinical and follow up study of 25 manic depressive cases treated with lithium carbonate. Paper presented at the XXIX Annual Conference of the Ind. Psychiatric Society held at Calcutta.
- PRAKASH, R., SETHI, N. and SETHI, B. B. (1978). Lithium in affective disorder. *Ind. J. Psychiat.*, 20, 360.
- PRIEN, R. F., CAFFEY, E. M. JR. and KLETT, C. J. (1972). Relationship between serum lithium level and clinical response in acute mania treated with lithium. *Brit. J. Psychiat.*, 120, 409.
- SCHOU, M., AMDISEN, A. and TRAP-JENSEN, J. (1967). Svaer lithiumfergiftning. Meddelelse om 8 tilfaelde. *Nord. Med.*, 78, 831.
- VENKOBA RAO, A. and HARIHARASU RAMANIAM, N. (1978). Lithium treatment of affective disorders—Certain observations *Indian J. Psychiat.*, 20, 304-309.