

Serum Lithium in Patients in Remission of Bipolar Disorder

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Abstract

Introduction: Bipolar affective disorder a chronic, and highly disabling psychiatric disorder is one of the leading causes of disability and is estimated to affect more than 1% of the global population irrespective of origin, ethnicity, nationality or socioeconomic status. The effectiveness of lithium in mania and psychotic excitement was proven first proven in 1960 and since then lithium is considered to be a gold standard treatment for bipolar disorder.

Material And Method: A total of one hundred thirty five patients with bipolar disorder were enrolled in a prospective study to analyze the serum lithium levels on maintenance dose of lithium. After ethical clearance data was collected from patients attending BG Hospital and Research Centre from July 2013 to July 2019. The patients who were on maintenance treatment with different doses of lithium only were included. These patients were tested for serum lithium concentration as per lithium monitoring guidelines. Serum Lithium, serum electrolytes, height and weight of the patients were recorded. The psychiatric diagnosis was made according to the ICD-10 criteria. Data were computed and analyzed by using SPSS version 21. Parametric and non-parametric statistical technique was applied wherever appropriate.

Results: The minimum efficacious serum lithium level in the long-term treatment of bipolar disorder was found at 0.16 mmol/l and maximum serum levels was 1.51 mmol/l. The mean serum lithium level was 0.596 mmol/l with standard deviation of 0.237 mmol/l.

Conclusion: There is substantial variation in between the serum lithium levels of patients in remission on long term treatment. The uncertainty about the most efficacious serum lithium level for the long-term treatment of bipolar disorder leads to the suggestion of the treatment of individual patients to be based on clinical response rather than on serum lithium levels.

Keywords: BPAD, Serum lithium Level, Remission

INTRODUCTION

Bipolar affective disorder a chronic, and highly disabling psychiatric disorder is one of the leading causes of disability and is estimated to affect more than 1% of the global population irrespective of origin, ethnicity, nationality or socioeconomic status.¹ Since John Cade first described lithium's antimanic properties in 1960 in manic illness² and therapeutic role in resolving "psychotic excitement" lithium has become a gold standard treatment for bipolar disorder, with evidence supporting its role in

acute mania, depression and prophylactic treatment.³

At the beginning of bipolar patients' treatment with lithium, it is often necessary to adjust the dosage as fast as possible. The recommended serum level to obtain a beneficial effect in bipolar disorder also varies with different guidelines while the general dictum is to maintain the serum lithium concentration at the range of 0.5-1.2 mmol/l.⁴ It is believed that inappropriate dosage can entail a poor control of

symptoms and potentially dangerous side effects.

Remission in BPAD is defined as absence or minimal symptoms of both depression and mania at least for one week, while sustained remission requires at least eight consecutive weeks of remission and as many as 12 weeks.⁵

In our routine practice in Nepal it is not always feasible to monitor serum lithium levels because of inability to maintain the regular follow up, compliance issue and unavailability of service to measure serum lithium etc. This study aimed to find out the serum lithium levels in patients with BPAD, currently in remission as per the ICD-10 criteria.

MATERIAL AND METHOD

This was prospective, and observational study performed on adult patients of either gender aged between 18 to 75 years and who were diagnosed as bipolar disorder, receiving Lithium as treatment and currently in remission and consenting to be a part of the study. The data was collected after due ethical clearance from patients attending BG Hospital and Research Centre Pvt. Ltd from July 2013 to July 2019. Patients who had co-morbid psychiatric illness, substance induced mood disorder, history of any other major medical or neurological disorders, patients who were pregnant, patients receiving diuretics, steroids, angiotensinogen converting enzyme inhibitors, angiotensin II receptor antagonists and non-steroidal anti-inflammatory drugs, and nausea/vomiting/diarrhea or other conditions leading to salt/water depletion were excluded. All patients were included in the study after taking written informed consent. After collection of the socio-demographic profiles, height, weight, dosage of lithium carbonate were recorded. Blood samples were drawn 12 hours (+/-) half hour from the last dose of the medication and evaluated for serum lithium concentration in accordance with the lithium prescribing and NICE PSA005, 2009.⁶ Flame photometric method was used to test the sample on Elyte-3i electrolyte analyzer. The gathered information was tabulated and statistical analysis performed. Data were analyzed at the end of study by applying paired and unpaired t test and Pearson Parametric Correlation tests using Statistical Package for Social Sciences

(SPSS), Inc., and Chicago, Illinois, USA version 21 for Windows. The differences between the groups were considered significant if the p-value were less than 0.05.

RESULT

The total numbers of participants of the study were 135. Out of which the majority were males 63% (n= 85) while 37% were female (n= 50). Average age of the patients of the study was 31.49 years with a mean weight of 55.83 kgs and mean BMI of 24.96. The prescribed dosage of lithium ranged from 300 mg per day to 1200 mg per day with a mean dosage of 938.52 mg per day.

The minimum efficacious serum lithium level in the long-term treatment of bipolar disorder was found at 0.16 mmol/L and maximum serum levels was 1.51 mmol/L. The mean serum lithium level was 0.596 mmol/L with standard deviation of 0.237 mmol/L. The details of the descriptive statistics have been further more explained in table 1.

Table 1: Descriptive characteristics of samples

| | N | Minimum | Maximum | Mean | Std Deviation |
|---------------|-----|---------|---------|--------|---------------|
| Age | 135 | 13 | 63 | 31.49 | 11.797 |
| Weight (Kg) | 135 | 31.0 | 90.0 | 55.83 | 10.580 |
| Height (Cm) | 135 | 145.0 | 170 | 159.56 | 6.413 |
| BMI | 135 | 13.61 | 40.27 | 24.96 | 4.813 |
| Dose/day | 135 | 300 | 1200 | 938.52 | 142.039 |
| Serum Lithium | 135 | 0.16 | 1.51 | 0.596 | 0.237 |
| Na+ | 135 | 135 | 150 | 141.57 | 3.495 |
| K+ | 135 | 3.1 | 5.7 | 4.021 | 0.610 |
| Valid N | 135 | | | | |

In our study we observed the serum lithium level was negatively co-related with weight (kg). (Pearson correlation -.196, P value 0.023) and positively correlated with dosage (Pearson correlation .232, P value 0.007)

Table 2 : Correlations of Serum lithium levels with Doses

| Correlations | | | |
|------------------------|---------------------|----------------|-----------|
| | | S lit (mmol/l) | dose /day |
| Serum lithium (mmol/l) | Pearson Correlation | 1 | .232** |
| | Sig. (2-tailed) | | 0.007 |
| | N | 135 | 135 |

*. Correlation is significant at the 0.05 level (2-tailed).

** . Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION:

In the present study we found that serum lithium levels were positively correlated with lithium dosage by Pearson's correlation test. Various studies have suggested that body size, age and renal function are factors associated with lithium clearance.⁷ Further more loss of fluid and sodium ions could be associated with lower lithium clearance.⁸ The serum lithium levels in patients and the factors related are still incompletely understood and remain a subject of debate.⁹

Keeping the fact that gender distribution in bipolar disorders does not vary consistently, number of male patients outnumbered female patients. Numerous equations and dosage prediction methods have been proposed to help the clinician identify appropriate lithium doses for desired therapeutic concentrations.¹⁰ The American Association Department of Drugs (1973) specially quoted that maintenance levels should not exceed 0.8mmol/l.^{10,11} The serum levels considered effective for prevention of relapse in mood disorders is at 0.6 to 1.0 mmol/l.^{12, 13, 14.}

This study provides evidence of direct relationship between dose and serum concentration which is similar to results demonstrated by Tika Ram et al.¹⁵

Lithium is an effective prophylactic treatment for bipolar disorders with dose ranging from 300 mg/day and serum concentration 0.16 mmol/l up to dose of 1200 mg/day with serum concentration 1.51 mmol/l without much

serious side effects hampering the functioning of patient. However, mean effective dose of 900mg targeting mean serum lithium level of 0.6mmol/L, though not established as safe by this study, could be innocuous options in treatment plan.

CONCLUSION:

There is substantial variation in between the serum lithium levels of patients in remission on long term treatment. The uncertainty about the most efficacious serum lithium level for the long-term treatment of bipolar disorder leads to the suggestion of the treatment of individual patients to be based on clinical response rather than on serum lithium levels.

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