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Bipolar Affective Disorder

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ASSESSING LITHIUM LEVELS AFTER ONCE DAILY DOSAGE IN PATIENTS OF BIPOLAR AFFECTIVE DISORDER IN A CLINICAL SETUP

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ABSTRACT

Objective: To determine the variations in serum lithium levels in 24 hrs and to establish the time required for lithium to reach its peak levels after once daily dosage.

Study Design: Case series study.

Place and Duration of Study: This study was carried out at a tertiary care hospital, from Dec 2016 to Jun 2017.

Patients and Methods: One hundred patients of Bipolar Affective Disorder who were receiving lithium for treatment or prophylaxis were selected randomly from OPD (with negative history of renal co-morbidity and intake of diuretics). These selected patients were admitted in hospital for five days with their consent. These admitted patients were given 800mg of lithium under supervision ensuring adherence to single dose lithium ingestion for five days. During their admission a brief history regarding their illness was taken meanwhile patients were screened for any possible renal co-morbidity. After 5 days of monitored lithium ingestion serial serum samples of the patients in the study were collected with their consent. Samples were collected after 0, 2, 4, 6, 12, 18 hours of ingestion of a single dose (800mg) of slow release lithium carbonate.

Results: Serum lithium levels in 77% (n=68) of samples taken at 0hrs ranged from 0.2-0.5meq/ltr, in 61.7% (n=50) of second sample taken at 2hrs ranged from 0.3-0.6meq/ltr, after 4hrs 74.3% (n=61) of samples serum lithium ranged 0.5-1.0meq/ltr, indicating further increase in serum lithium levels. Six hours after the ingestion of lithium 85% (n=70) of samples revealed increased serum lithium level to the range of 0.5-0.9meq/ltr. Twelve hours after the ingestion of lithium 77.7% (n=70) had serum lithium level 0.4-0.7meq/ltr indicating that now levels had started to fall. After 18 hours in 80.2% (n=70) samples lithium levels were 0.3-0.6meq/ltr showing downward slope which was still higher than baseline.

Conclusion: Appropriate lithium level can only be obtained when serum sample is taken at appropriate time. Appropriate time of sample collection for serum lithium level is twenty four hours after the last dose of lithium if slow release preparation is being used.

Keywords: Clinical settings, Lithium, Pharmacokinetics.

INTRODUCTION

Mood refers to a sustained emotional state that can be normal, elevated or depressed[1]. High cost, extensive morbidity and availability of effective treatment combine to make mood disorder a matter of clinical and public health importance[2].

Over the course of this century lithium has evolved from a drug for short-term and prophylactic management of the disorder to the mainstay of treatment. Lithium is a monovalent ion, and lightest amongst the alkali metals (group IA of the periodic table)[3]. Serum lithium level peaks in one to one-and-a-half hours for standard preparation and in four to four-and-half hours for controlled release preparations. Its half life is 20 hours and equilibrium is reached after 5-7 days of regular intake in patients with normal renal functions[4,5].

Therapeutic drug monitoring is an established tool that gives clinicians greater control over the medication dose and helps in determining patient compliance and detecting early signs of lithium toxicity[6,7]. There have been

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studies proving early and comprehensive evaluation and management of lithium intoxication, requiring serum lithium estimation[8].

Currently in Pakistan the standard therapeutic regimen and procedures to assess lithium level is to use a single dose of slow release lithium carbonate preparation followed by collection of blood sample after 12 hours of ingestion of the dose. Taking into account hot and humid temperate weather of Pakistan and the metabolism of Pakistani nation, there is a need to undertake a study of pharmacokinetics of lithium in a section of hospital based population, to determine the optimum time for collection of sample for determining the therapeutically significant serum lithium level after a single dose of lithium. Single dosing is useful where there are compliance issues and when prolonged medication is a requirement such as in mania and bipolar illness.

The aim of this study is to determine the ideal time for collection of blood sample for assessing the steady state and peak serum lithium levels.

PATIENTS AND METHODS

This case series study was conducted in Combined Military Hospital Kharian from Dec 2016 to Jun 2017. After careful history both psychiatric and medical (to rule out concomitant use of other drugs like NSAIDs, diuretics and/or other mood stabilizers which might affect serum lithium levels) and medical and psychiatric evaluation (to rule out thyroid and/or renal conditions) one hundred patients of Bipolar Affective Disorder were selected from OPD using convenience (non probability) sampling technique. These patients were receiving Lithium for treatment or prophylaxis. After obtaining consent selected sample of patients were admitted in Psychiatry ward for five days. For the purpose of this study these admitted patients were given 800mg of Lithium orally for five days under supervision ensuring adherence to single dose regimen. After 5 days of monitored lithium ingestion serial serum samples of patients in study were collected with the consent of the individuals. Samples were collected after 0, 2, 4, 6, 12, 18 hours of ingestion of a single dose (800 mg) of slow release lithium carbonate. Obtained data was analyzed using statistical package for social sciences (SPSS).

RESULTS

Out of hundred selected patients eighty one gave consent for participation in the study, ten refused to have any involvement in any kind of study while nine individuals did not report on the due date after agreeing and giving consent. Age of the patients included in the study was between 21-53 years with mean age 34 years. Out of eighty one patients who participated in the study, 67 were males (82-7%) whereas 15 (18.5%) were females.

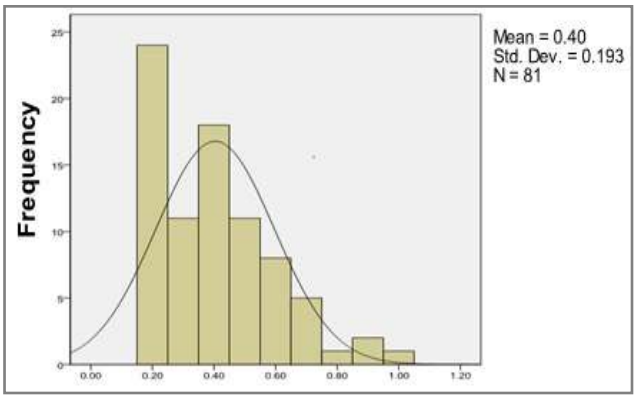

Figure-1: First sample taken 0 hours before taking next dose.

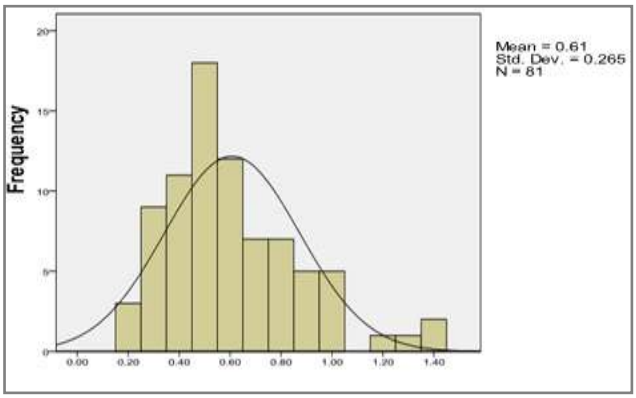

Figure-2: Second sample, taken 2 hours after taking dose.

First sample noted at 0 hours that was obtained 24 hours after the last dose of lithium slow release preparation showed variability of

lithium in serum ranging from 0.2-1.0meq/ltr. 30% had serum lithium level of 0.2, 21% had 0.4 while 13.6% had 0.5meq/ltr as shown in fig-1.

Second sample obtained 2 hours after lithium ingestion showed a range of lithium level from 0.2-1.4meq/ltr. 22.2% had serum lithium level of 0.5meq/ltr, 14% had 0.6, 13.6% had 0.4 while 11.1% had 0.3meq/ltr as shown in fig-2.

Four hours after the ingestion of lithium serum lithium levels ranged from 0.2-1.5meq/ltr.

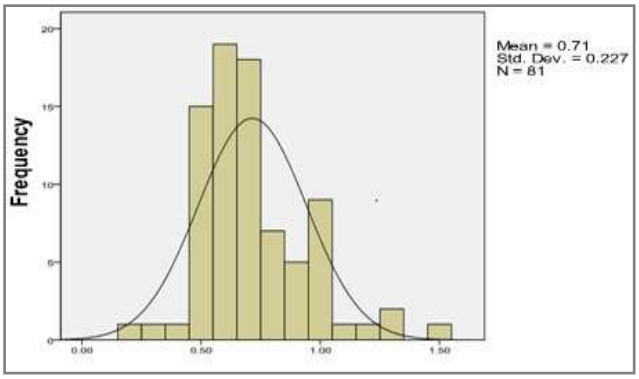

Figure-3: Third sample taken 4 hours after taking dose.

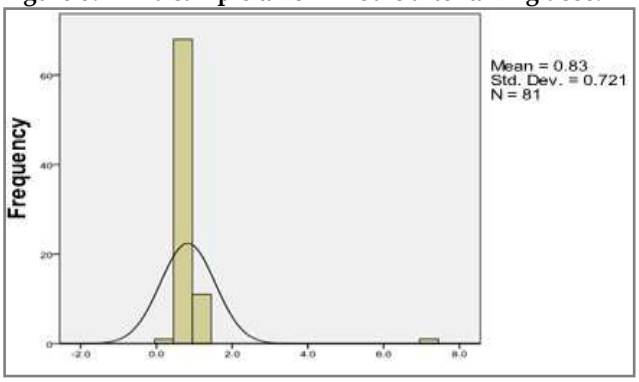

Figure-4: Fourth sample taken 6 hours after taking dose.

23.5% had serum lithium level of 0.6meq/ltr, 22% had 0.7, 18.5% had 0.5 while 11.1% had 1.0meq/ltr as shown in fig-3.

Six hours after the ingestion serum lithium levels ranged from 0.2-1.30meq/ltr. 39.5% of samples had serum lithium level of 0.7meq/ltr, 12.3% had 0.5, 12.3 had 0.9 while 11.1% had 0.8meq/ltr as shown in fig-4

After 12 hours serum lithium levels ranged from 0.3-1.4meq/ltr. 28.4% of samples had level of 0.6meq/ltr, 13.5% had 0.7, 16% had 0.4 while 14.8% had 0.5meq/ltr of serum lithium as shown in fig-5.

Eighteen hours after the ingestion of lithium serum lithium levels ranged from 0.2-1.3meq/ltr. 24.7% of samples had 0.4meq/ltr, 22.2% had 0.5, 17.3% had 0.6 while 16% had 0.3meq/ltr of serum lithium as shown in fig-6.

In summary 77% of samples obtained at 0 hours range of serum lithium level was 0.2-0.5meq/ltr, after two hours 61.7% of samples had

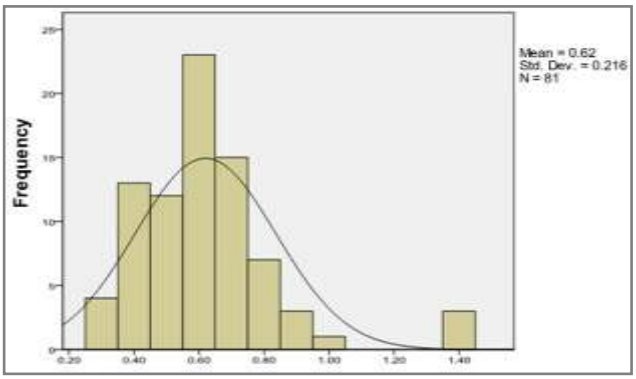

Figure-5: Fifthe sample taken 12 hours after taking dose.

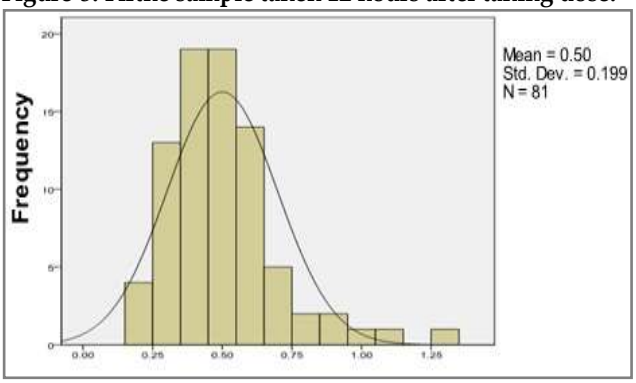

Figure-6: Sixth sample taken 18 hours after taking dose.

range of 0.3-0.6meq/ltr, after 4 hours 74.3% of samples had range of 0.5-1.0meq/ltr, after six hours 85.1% of samples had range of 0.5-0.9meq/ltr, twelve hours after ingestion of lithium 77.7% of samples had range of 0.4-0.7meq/ltr. After 18 hours there was further decline in serum lithium levels with 80.2% of samples having range of 0.3-0.6meq/ltr but still higher than the base line as shown in fig-7.

DISCUSSION

For Bipolar Affective Disorder, that affects 5% of population, lithium remains the corner-

stone of maintenance therapy despite growing use of other mood stabilizers[9]. Lithium is rapidly and completely absorbed with serum concentrations peaking in one to one and half hours with standard preparations and in four to four and half hours with slow and controlled release forms[10]. The elimination half life of lithium is about eighteen to twenty-four hours. Lithium is distributed throughout the body although rate and extent of entry into the tissue varies. Lithium has been measured in virtually every body fluid but only blood (serum or plasma) is used in clinical practice. Essential to interpreting serum lithium level is knowing the sampling interval (the time between the last dose and the drawing of blood), the dose form, and the dosage schedule[11,12]. The blood concentrations obtained an hour or so after a dose is considerably higher than those obtained after a long sampling interval. The twelve interval that has been adopted as standard has been defined as follows: (1) blood should be drawn in the morning twelve hours after the last dose, (2) a multiple dose regimen should be used, and (3) a steady state condition should exist. Twelve hour serum concentration will be higher with single as opposed to multiple daily dosing. Even when these guidelines are followed, the serum level may fluctuate from measurement to measurement, reflecting factors such as dietary sodium, mood state, activity level, body position and improper sampling[13,14].

This study was conducted to evaluate whether the slow release lithium carbonate provides steady state plasma lithium level after twelve hours of ingestion, and whether sample collection after twelve hours is proper time for plasma lithium assessment?

This study is expected to help the clinicians to operate safely by helping them to ascertain the appropriate time for sample collection. It will help clinicians in drawing appropriate inference of the serum lithium levels that are seen at different times after the ingestion of lithium. It will also guide the clinicians in adjusting the dose appropriately with clear understanding of varied serum levels at varied times

This study clearly demonstrates that there is rise of serum lithium levels in first two hours after the ingestion of slow release lithium carbonate. Serum lithium levels reach their peak in four hours that is sustained as plateau depicted in readings of third and fourth samples. After twelve hours of ingestion of slow release lithium carbonate serum lithium levels show a decline. Here it is important to note that although serum lithium levels have fallen, but still the levels are higher than the base line. Results of the samples taken eighteen hours after the ingestion of lithium show further decline in the lithium levels but still the levels are higher and do not reach the baseline. Variation in the serum lithium level among the samples taken during the same time period in different patients can be noted. Based on the results of this study it is recommended that while using lithium carbonate preparation one should make note that either it is standard or slow release preparation because taking serum sample twelve hours after the last dose is helpful in determining accurate serum lithium level only if standard lithium preparation is used but it would be misleading for slow release lithium preparation. Therefore it is recommended that if slow release lithium preparation is being used it is prudent to take serum sample twenty four hours after the ingestion of last dose to get accurate readings.

CONCLUSION

Appropriate lithium level can only be obtained when serum sample is taken at appropriate time. Appropriate time of sample collection for serum lithium level is twenty four hours after the last dose of lithium if slow release preparation is being used.

LIMITATION OF STUDY

Variables like dietary sodium, mood state, activity level, body position and improper sampling were confounding variables and were not controlled. Effects of other concomitant drugs used by patients were also not controlled. Sampling technique was convenient non probability.

Clinical Implications

This study will help the clinician to operate safely.

It will help clinician in ascertaining the appropriate time for sample collection and will help clinician in drawing appropriate inference of the serum lithium levels that are seen at different times after the ingestion of lithium.

This study will also guide the clinician in adjusting the dose appropriately with clear understanding of varied serum levels at varied times.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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