Indian J. Psychiat. (1989), **31**(1), 70—72

HOW RELIABLE IS 24 HOUR SERUM LITHIUM LEVEL AFTER A TEST DOSE OF LITHIUM IN PREDICTING OPTIMAL LITHIUM DOSE?

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SUMMARY

57% of a group of 35 patients treated with Lithium Carbonate at dosages predicted by the nomogram suggested by Cooper et al (1973) failed to reach therapeutic levels of serum lithium. This finding casts serious doubts on the usefulness of the claim by Cooper at al (1973 & 1976) that 24 hour serum lithium level after a test dose of 600 mg. lithium can predict the daily lithium dose.

The effectiveness of lithium salts in the treatment of and prevention of affective psychoses has led to its widespread use. The effective serum level of lithium is generally considered to be between 0.6 to 1.2 mEq/litre (Cooper et al, 1973 & Naiman et al, 1981). Several workers have tried to develop methods which will help the clinician to predict the dosage requirements of the individual patient within reasonable limits. One such method was described by Cooper et al (1973) which was claimed to be helpful to the physician to predict the dose of lithium required to maintain a steady state of serum lithium level of 0.6 mEq/litre to 1.2 mEq/litre based on the serum lithium level in a single sample of blood drawn 24 hours after administration of 600 mg. of lithium. Further studies by Cooper et al (1976) and Gengo et al (1980) have confirmed the reliability of the method. A recent study by Fava et al (1984) showed that the test was able to predict the lithium dosage correctly in 96.6% of the 30 patients they studied. However other workers like Naiman et al (1981) found that about 30% of their patients failed to achieve the defined steady state range when given lithium at the dose predicted on the basis of Cooper et al's nomogram.

The term loading dose used by Cooper et al., (1973) and Fava (1984) to describe this method of is inaccurate since this method was designed only to eliminate slow dosage and does not alter the rate of drug accumulation. The 600 mg. dose of lithium given initially before assessment of 24 hour serum lithium level may be referred to as a 'test dose' instead.

Considering the steadily increasing clinical use of lithium and the desirability of achieving a therapeutic level of serum lithium in as short a time as possible, it was felt that if the reliability of the method suggested by Cooper et al (1973) could be established in Indian patients it would be of great benefit in reducing the duration of the patient's and his family's suffering due to his symptoms and in cutting down the days of hospitalisation and the expenses for treatment and so the present study was undertaken.

METHOD:

35 adults, 24 males and 11 females, of the age range of 18 to 65 years

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diagnosed to be having Manic Depressive Psychosis, manic type and circular type (currently being in the manic or depressed phase) as defined by ICD IX (1978) were included in the study. Of the thirty five patients, 7 were given lithium for the control of the current manic phase whereas in the other 28 it was given as a prophylactic against future episodes of affective psychoses because of the past history of recurrent manic or circular episodes. All the patients were also on antipsychotic drugs (Chlorpromazine or Haloperidol) or on antidepressant drugs (Imipramine or amitriptyline). Physical examination and estimation of serum creatinine, blood urea, thyroid function tests, microscopic examination of urine and qualitative test of urine for albumin and sugar were done in all patients before taking them up for the study and results of all the above tests were within normal limits. None of the patients in the study had recieved lithium earlier.

All the patients studied were being treated as inpatient and their compliance with medication were ensured by the relatives who stayed with patients in the hospital and also by the staff nurse who administered the drug. On the first day 600 mg. (two 300 mg. tablets) of lithium carbonate was given to the patient followed by about 100 c.c. of water and the staff nurse made sure that the patient swallowed this medicine completely. Exactly 24 hours later 6 c.c. of blood was drawn and immediately transferred to the Clinical Biochemistry Iaboratory where the estimation of serum Lithium level was done accurately to the second decimal point. The accuracy of the technique had been evaluated in a previous study (Kuruvilla et al, 1977) and also by estimating the lithium level in the same serum sample by two other laboratories. On the basis of the 24 hour serum concentration and nomogram provided by Cooper et al (1973) a dose regimen was selected and the patient was started on that dose of lithium the same day. After the patient has been on the same dose for five full days, blood was again drawn exactly 12 hours after the last dose of lithium and serum lithium estimated.

RESULTS:

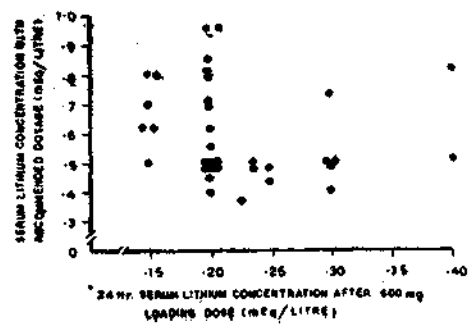
The 24 hour serum lithium level after a test dose of 600 mg. of lithium carbonate varied from 0.15 to 0.40 mEq/litre, the predicted dose varied from 300 mg. twice a day to 300 mg. four times a day. The level achieved with the predicted dose varied from 0.37 to 0.95 mEq/litre as shown in the scatter diagram.

Among the 35 patients studied only 15 (42.86%) achieved a serum level 0.6 to 1.2 mEq/litre with the dose predicted by the nomogram of Cooper et al/(1973) The 20 (57.14%) who failed to achieve

TABLE I

24 Hours Lithium level after single dose	Reached expected level	Failed to reach expected level
0.15 to 0.19* (N=6)	5	1
0.20 to 0.23* (N=20)	8	12
0.24 to 0.30** (N=7)	1	6
More than 0.30 ** (N=2)	2	1

Predicted dose 300 mg tid ** bid.



therapeutic level required additional lithium ranging from 150 mg. to 600 mg. per day to attain a serum level of 0.6 to 1.2 mEq/litre.

Correlation between the serum lithium level after single 600 mg. test dose and the level obtained on the predicted dose of lithium is not significant ($r=0.12$). The observed distribution of serum lithium on the predicted dosage is significantly different from the expected level ($p<0.001$) as seen on the test of goodness of fit.

DISCUSSION:

The present study fails to confirm the predictive value of the serum lithium level after a test dose of 600 mg. of lithium to determine the daily dose of lithium required by a patient to achieve the therapeutic level of 0.6 to 1.2 mEq/litre. Our findings are in agreement with Naiman et al (1981) who found that 30.7% of their patients failed to achieve steady state range.

Cooper and Simpson (1976) and Fava et al (1981) suggest that the possible reasons for aberrant results may be(1) patient not ingesting all the medication(2) blood sample not being collected at the correct time and (3) the laboratory not being capable of accurate estimation. The present study took precautions to avoid the first two problems. Our previous experience with the laboratory and comparison of our results with other laboratories gave enough grounds to accept the laboratory results as dependable. But the possibility still remains that the difference in the technique used to determine serum lithium level may be contributory to the difference in our observation from that of others like Cooper et al (1973), Fava et al (1984)and Gengo et al (1980). In all these reports serum was analysed by atomic absorption spectro-photometer whereas in the present study flame photometer was used. However both methods are reported to give satisfactory results and when both techniques are applied to the same samples the results are very comparable (Coombs. 1975; Lipmann et al, 1981). In our laboratory we are using atomic absorption spectrophotometer now. At the time of changing over to this from flame photometer we made several comparisons of the results with both techniques with same serum samples and found that results are very similar.

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