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## Utility of Measuring Red Blood Cell Efflux Rates of Lithium in the Therapeutic Management of Manics

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### *Abstract*

The rate of efflux of lithium from red blood cells was studied to assess its utility in predicting the response to lithium therapy in manics. It was noted that the efflux rates were lower in manics who responded to therapy with lithium. It was also noted that there were significant alterations in efflux rates of some manics who developed toxic side effects.

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Key words -

**Lithium,**

**RBC,**

**Efflux rates,**

**Manics,**

**Half-life**

In the therapeutic management and subsequent prophylaxis, the use of lithium salts have received universal acclaim. In a majority of the manic patients, lithium is highly effective (responders). However, in a small group of approximately 20 per cent, lithium salts appear to be ineffective (non-responders). A report of studies made to find out whether red blood cells efflux rates of lithium could be used to differentiate the two groups and evaluating its utility in those who develop toxic side effects, is made in this paper.

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### **Material and Methods**

The clinical material used in this study was obtained from among patients coming for consultation to the psychiatry department at this centre. Forty manic patients were available for this study. In all these cases blood samples were collected in vials containing ammonium heparin. The red blood cells were separated by centrifugation, washed thrice with magnesium chloride solution (115 mM) and incubated for 60 minutes at 37° C in a medium containing lithium chloride (40 mM) and sodium chloride (10 mM). The cells were separated and washed as before. One aliquot was taken for lithium assay. The

other aliquot was divided into four batches and kept for incubation for 1, 2, 3 and 4 hours in a medium containing lithium chloride (15 mM), sodium chloride (135 mM) and potassium chloride (5 mM). At the end of respective period of incubation, the cells were separated and washed. The cells from baseline and subsequent aliquots were hemolyzed with distilled water (1:10) and lithium is determined by using a Flame photometer [2]. The erythrocyte lithium concentration at 0, .12, 3 and 4 hours is used for determining the half life.

The long linear relationship between two parameters, viz:

- (1) erythrocyte concentration, and
- (2) time, is necessary for determination the half life of efflux [3].

This is done by calculation of the rate of efflux of lithium from RBC. The log erythrocyte lithium concentrations are plotted against time of efflux (in hours) on a graph paper. The slope of each curve is calculated and from this the half-time (in hours) of lithium efflux from RBC is determined for each patient.

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## Results and Discussion

In the 40 patients included in this study lithium was administered for four weeks at an adequate dose so as to achieve serum levels between 0.9-1.4 mEq/L. At the end of the period if the initial clinical symptoms, as scored on a mania scales [4], had been relieved by 75 per cent, the patients were considered as responders. It was found that in these responders, the rate of efflux of lithium from red blood cells are different from that noted in responders as indicated below:

***Half life.***

Mean & S.D.

***of lithium efflux from red blood cells***

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This was attributed to the differential rate in fall of the levels. The rate of lithium efflux from red blood cells is much lower in manics who get benefited from administration of lithium which is reflected by the long half life of efflux. Very low efflux rates are noted in responders.

It was noted that in some manics who occasionally developed toxic side effects, even at therapeutic levels of lithium, the red blood cells had lithium in considerable amounts.

The fact that very low efflux rates characterize responders would merit further studies since if nonresponders could be identified it would save time and alternate therapy started and also avoid them from being exposed to a potentially toxic drug.

The fact that the responders differ from nonresponders in having differential efflux rates and also the fact occasionally toxic cases have lithium within their red blood cells over protracted period of times (even after discontinuance of therapy) would indicate alterations in membrane transport. Among the major pathways for lithium transport across cell membranes are the ouabain sensitive Na-K pump; the Na-Li counterflow and passive transport. The Na-Li counterflow is the one which influences lithium

transport across membranes. The present findings are in agreement with the earlier reports of Dorus et al [5].

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