Lithium Stability Study

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Introduction

Lithium is a mood stabilizing drug, primarily used to treat bipolar disorders. It is highly toxic & has a narrow therapeutic window, hence close monitoring is required.

Currently the Northern Trust uses Roche Cobas 501 to measure serum lithium levels. Roche states that the specimen should be separated from cells if storage for > 4 h is anticipated. This can prove challenging due to transport delays. Centrifuging at source may be an alternative option. There are limited studies[1][2] that evaluated the stability of Lithium in whole blood.

Aim

This study aims to evaluate the impact of time delays on the stability of Lithium in whole blood so as to facilitate defining acceptable pre-centrifugation delays in transport.

Method

Samples were collected randomly from 22 patients on lithium treatment who were attending the Coleraine Mental Health clinic. Two samples were collected from each patient, a labelled gel & an unlabelled clotted sample. The labelled gel tube was centrifuged immediately upon receipt, analysed and reported as usual for lithium. Unlabelled samples were left out at room temperature. Every 2 hours the sample was mixed and a small aliquot of whole blood was centrifuged & analysed. The same procedure was carried out throughout the study. Each time point of analysis consisted of 0, 2, 4, 6, 8, 10, 12, 18 (started at week 2 & onwards) and 24 hours.

The stability of lithium was determined by comparing results to the baseline (T=0) result for each sample. A mean % of each sample was calculated using the following formula; mean bias% = 100 × (measured value – T=0)/ T=0. An Analytical Change Limit (ACL) of 15% was used to determine stability. ACL is equal to $1.96 \times \sqrt{2} \times Cva$ (CVa is the inter-assay imprecision calculated from Randox Control value)

Results

Sample no.	T=0	T=2	T=4	T=6	T=8	T=10	T=12	T=18	T=24
1	0.81	0.88	0.84	0.85	0.84	0.85	0.83		0.95
2	0.32	0.32	0.39	0.33	0.39	0.35	0.36		0.41
3	0.57	0.51	0.57	0.53	0.55	0.55	0.57		0.6
4	0.41	0.42	0.38	0.43	0.41	0.41	0.39		0.47
5	0.66	0.65	0.7	0.68	0.66	0.65	0.67		0.78
6	0.95	0.97	0.97	0.95	0.95	0.97	0.93	0.9	0.98
7	0.53	0.57	0.57	0.59	0.6	0.58	0.59	0.55	0.65
8	0.87	0.82	0.86	0.89	0.84	0.88	0.83	0.85	0.92
9	0.55	0.55	0.57	0.58	0.57	0.58	0.57	0.57	0.65
10	0.93	0.91	0.91	0.91	0.9	0.9	0.91	0.9	0.99
11	0.45	0.43	0.44	0.45	0.43	0.45	0.43	0.44	0.52
12	0.84	0.83	0.82	0.8	0.81	0.81	0.83	0.81	0.9
13	0.77	0.84	0.73	0.74	0.78	0.74	0.76	0.77	0.76
14	0.52	0.58	0.5	0.5	0.54	0.48	0.48	0.51	0.53
15	0.77	0.79	0.75	0.77	0.79	0.73	0.75	0.81	0.76
16	0.74	0.66	0.62	0.65	0.65	0.61	0.65	0.64	0.65
17	0.6	0.49	0.5	0.49	0.5	0.5	0.48	0.49	0.5
18	0.49	0.43	0.4	0.38	0.37	0.39	0.38	0.38	0.43
19	0.56	0.47	0.48	0.48	0.51	0.46	0.45	0.49	0.48
20	0.77	0.76	0.74	0.76	0.74	0.76	0.73	0.77	0.76
21	0.34	0.33	0.36	0.34	0.32	0.31	0.36	0.35	0.36
22	0.45	0.42	0.43	0.42	0.46	0.47	0.45	0.49	0.47
Mean	0.63	0.62	0.62	0.61	0.62	0.61	0.61	0.63	0.66
T test value		0.256	0.116	0.096	0.21	0.055	0.038	0.059	0.067
Significance (5%)		NS	NS	NS	NS	NS	Significant	NS	NS

Table 1 shows lithium results on 22 samples/24 hours. The mean &t test value are calculated for each time interval &using a p value of 0.05 to determine its significance.

Sample no.	T=0	T=2	T=4	T=6	T=8	T=10	T=12	T=18	T=24
1	0	0.07	0.03	0.04	0.03	0.04	0.02		0.14
2	0	0	0.07	0.01	0.07	0.03	0.04		0.09
3	0	-0.06	0	-0.04	-0.02	-0.02	0		0.03
4	0	0.01	-0.03	0.02	0	0	-0.02		0.06
5	0	-0.01	0.04	0.02	0	-0.01	0.01		0.12
6	0	0.02	0.02	0	0	0.02	-0.02	-0.05	0.03
7	0	0.04	0.04	0.06	0.07	0.05	0.06	0.02	0.12
8	0	-0.05	-0.01	0.02	-0.03	0.01	-0.04	-0.02	0.05
9	0	0	0.02	0.03	0.02	0.03	0.02	0.02	0.1
10	0	-0.02	-0.02	-0.02	-0.03	-0.03	-0.02	-0.03	0.06
11	0	-0.02	-0.01	0	-0.02	0	-0.02	-0.01	0.07
12	0	-0.01	-0.02	-0.04	-0.03	-0.03	-0.01	-0.03	0.06
13	0	0.07	-0.04	-0.03	0.01	-0.03	-0.01	0	-0.01
14	0	0.06	-0.02	-0.02	0.02	-0.04	-0.04	-0.01	0.01
15	0	0.02	-0.02	0	0.02	-0.04	-0.02	0.04	-0.01
16	0	-0.08	-0.12	-0.09	-0.09	-0.13	-0.09	-0.1	-0.09
17	0	-0.11	-0.1	-0.11	-0.1	-0.1	-0.12	-0.11	-0.1
18	0	-0.06	-0.09	-0.11	-0.12	-0.1	-0.11	-0.11	-0.06
19	0	-0.09	-0.08	-0.08	-0.05	-0.1	-0.11	-0.07	-0.08
20	0	-0.01	-0.03	-0.01	-0.03	-0.01	-0.04	0	-0.01
21	0	-0.01	0.02	0	-0.02	-0.03	0.02	0.01	0.02
22	0	-0.03	-0.02	-0.03	0.01	0.02	0	0.04	0.02
Mean Diff	0	-0.012	-0.017	-0.017	-0.013	-0.021	-0.023	-0.024	0.028
Mean Diff (%)	0	-1.98	-2.73	-2.81	-2.13	-3.50	-3.73	-3.82	4.27

Table 2 shows mean bias difference for each time interval compared against T=0.
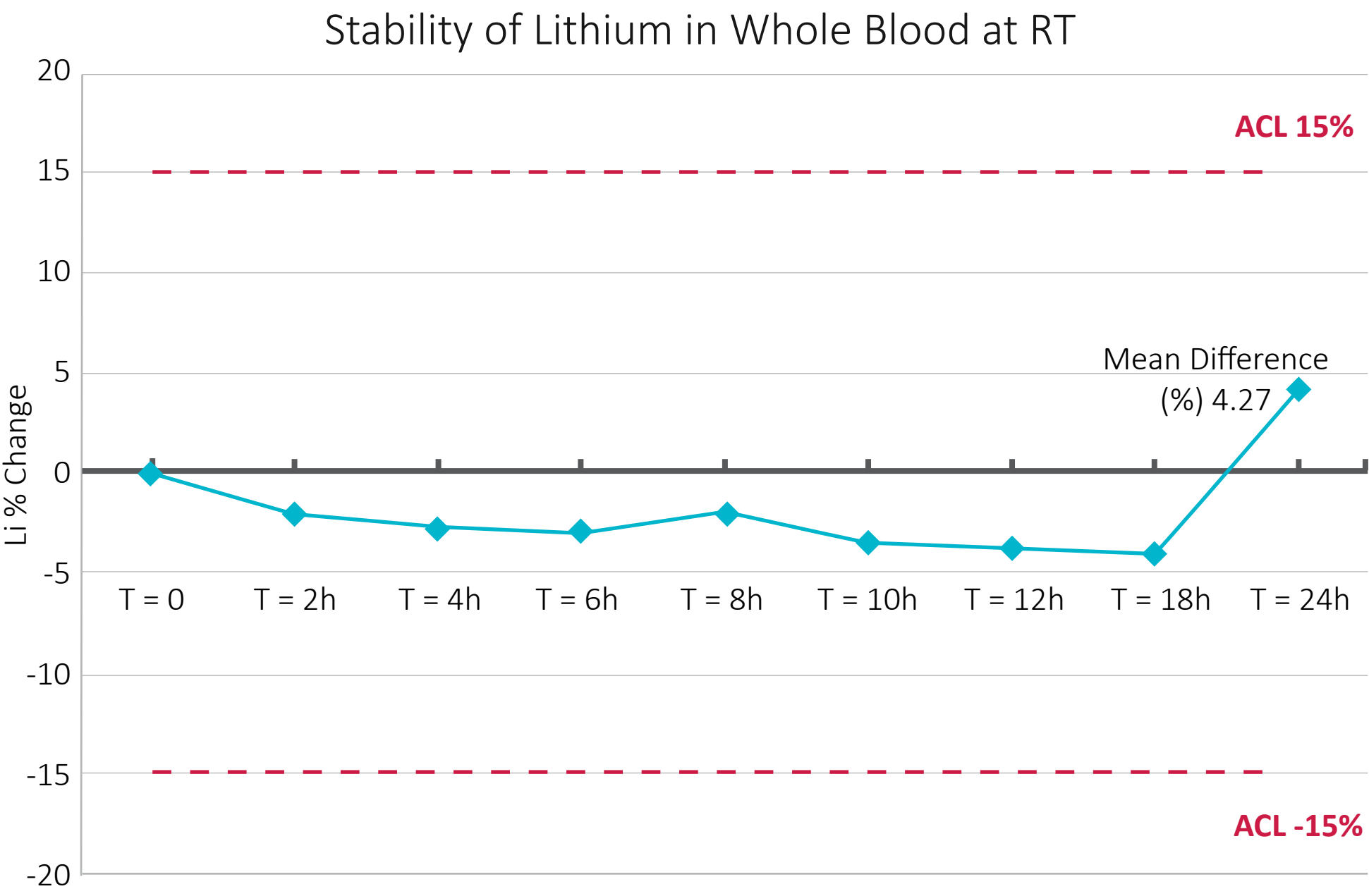

Figure 1 shows a graph of stability of Lithium over 24 hours using the mean difference for each time interval. This is compared against the ACL limit which is highlighted above.

Conclusion

- From the results, we conclude that lithium is stable for up to 24 hours at room temperature.
- Our studies disregard Roche suggestion that it is important to separate erythrocytes to rule out interference from lysed red cells without any in vitro studies of their own.
- The acceptable stability of lithium in whole blood can be extended from 4 to 24 hours before centrifugation.
- Transport delays in these samples should not impact on rejection for analysis, if processed in 24 hours, and will obviate the need for a centrifuge at source.

References

1. G Mulyran et al. Lithium Stability in clotted blood: storage guidelines. Clinical Chemistry. 1987 October
2. Sudhir K. Khandelwal et al. Stability of serum Lithium levels – Usefulness and Relevance in Indian Conditions. Indian J. Psychiat. 1981