Chapter IV

Results and Discussion

Characteristics of the patients and dosage regimen

The patients taking lithium who met the criteria of this study were evaluated. Forty-two patients who were admitted in the hospital were analyzed. Table VI showed the characteristics of the patients, table VII showed the dosage regimen administered to each patients. Maintenance dose of lithium was administered to the patients in three different patterns to maintain lithium blood level, the dosage regimen usually prescribed by physicians were 600 mg per day, 900 mg per day and 1200 mg per day. The percentage of patients taking various dosages of lithium were concluded in table VIII. The forty-two patients studied could be divided into two groups, one group of patients used lithium to control the manic episode while the other group of patients used lithium as adjunctive therapy with other drugs such as antipsychotics, antidepressants and anti-anxiety agents. Physicians in Srithunya Hospital tend to use conventional dosage regimen and have not applied pharmacokinetics to the lithium dosage regimen calculation.

Patients with psychiatric disorders usually use many groups of drugs for the best clinical improvement. Antipsychotics,antidepressants, anti-anxiety agents and other groups of drugs are always used concomittantly with lithium. In this study, all patients had taken lithium with antipsychotic drugs,

six out of forty-two patients had taken lithium with antidepressant drugs, and seven out of forty-two patients had taken lithium with anti-anxiety agents.

Table VI Demographic Data of Patients Taking Lithium carbonate.

Patient Number	Sex	Age (years)	Weight (kg.)	Height (cm.)
1	F	58	53	163.5
2	M	42	45	163
3	F	23	31.5	160
4	F	31	60	154
5	M	28	78	171
6	F	32	55	155
7	F	62	49	161
8	F	43	38	157
9	M	32	65	170
10	F	21	35	156
11	F	24	42	156
12	F	32	65	170
13	F	39	39	149
14	F	37	65	152
15	F	62	49	148
16	M	30	74	169
17	F	62	54	160
18	F	68	47	154
19	M	18	55	167
20	M	53	57	165
21	M	44	62	174
22	M	34	60	170
23	M	36	71	165

continued.....

Patient Number	Sex	Age (years)	Weight (kg.)	Height (cm.)
24	M	59	56.5	166
25	F	45	70	158
26	F	32	40	162
27	F	32	54	155
28	M	17	49	159
29	F	37	76	156
30	M	44	48	174
31	F	62	63	154
32	F	27	72	161
33	M	43	52	170
34	M	28	45	149
35	F	53	70	158
36	M	27	68	173
37	M	36	67	160
38	F	54	33	155
39	F	67	29	146
40	F	19	45	162
41	F	32	55	158
42	F	31	44	149

Males = 16 Females = 26

Age mean ± SD = 39.4286 ± 14.3580 , range = 17 - 68 years

Weight mean ± SD = 54.4286 ± 12.8811 , range = 29 - 76 kg.

Height mean ± SD = 160.3452 ± 7.5615 , range = 146 - 174 cm.

Table VII Dose of Lithium carbonate Administered to Each Patients.

Patient Number	Dose (mg/day)
1	600
2	900
3	900
4	900
5	900
6	900
7	900
8	600/900
9	900
10	600
11	600
12	900
13	1200
14	900
15	600
16	900
17	900
18	900
19	900/1200
20	900/1200
21	900

Patient Number	Dose (mg/day)
22	900
23	900
24	900
25	900/1200
26	1200
27	900
28	900
29	900
30	900
31	900/OFF
32	900
33	1200
34	900
35	900
36	900
37	900
38	900
39	900/OFF
40	900
41	900
42	900

/ before and after adjustment of lithium carbonate dosage

Table VIII Percentage of Patients Taking Different Dosage of Lithium carbonate.

Dosage of Lithium carbonate	Total number of patients (percent)
600 mg/day	5 (11.91)
900 mg/day	34 (80.95)
1200 mg/day	3 (7.14)

1. The blood lithium levels versus the dosage regimen

From this study, the dosage regimens were classified into three subgroups. The dosage regimen and the corresponding measured lithium concentration were recorded. Administered 600 mg lithium carbonate per day resulted in the measured lithium levels ranged from 0.42-0.90 mEq/L shown in table IX. The 900 mg lithium carbonate per day dose gave the measured lithium level to be 0.30-2.25 mEq/L shown in table X which was a very wide range indicated high interindividual variations among patients. After the 1200 mg lithium carbonate per day dose ,the measured lithium level was 0.70-1.10 mEq/L as shown in table XI.

Table IX Measured lithium steady state level of patients taking 600 mg lithium carbonate per day.

Patient Number	Age (years)	Dose (mg/kg/day)	Measured lithium level (mEq/L)
1	58	11.32	0.90
8	43	15.79	0.42
10	21	17.14	0.69
11	24	14.29	0.73
15	62	12.24	0.70
Mean	41.60	14.17	0.6880
SD	18.85	2.40	0.1722
Maximum	62	17.14	0.90
Minimum	21	11.32	0.42

Table X Measured lithium steady state level of patients taking 900 mg lithium carbonate per day.

Patient Number	Age (years)	Dose (mg/kg/day)	Measured lithium level (mEq/L)
2	42	20.00	0.62
3	23	28.57	1.56
4	31	15.00	0.86
5	28	11.54	0.58
6	32	16.36	0.59
7	62	18.37	1.03
9	32	13.85	0.69
12	32	13.85	0.54
14	37	13.85	0.46
16	30	12.16	0.57

continued.....

Patient Number	Age (years)	Dose (mg/kg/day)	Measured lithium level (mEq/L)
17	62	16.67	0.63
18	68	19.15	1.07
19	18	16.36	0.58
20	53	15.79	0.30
21	44	14.52	0.39
22	34	15.00	0.94
23	36	12.68	0.53
24	59	15.93	0.76
25	45	12.86	0.47
27	32	16.67	0.57
28	17	18.37	0.96
29	37	11.84	0.70
30	44	18.75	0.76
31	62	14.29	1.00
32	27	12.50	0.59
34	28	20.00	0.68
35	53	12.87	0.67
36	27	13.23	0.92
37	36	13.43	1.75
38	54	27.27	1.18
39	67	31.03	2.25
40	19	20.00	0.70
41	32	16.36	0.71
42	31	20.45	0.53
Mean	39.91	16.75	0.7982
SD	14.02	4.67	0.3984
Maximum	68	31.03	2.25
Minimum	17	11.54	0.30

Table XI Measured lithium steady state level of patients taking 1200 mg lithium carbonate per day.

Patient Number	Age (years)	Dose (mg/kg/day)	Measured lithium level (mEq/L)
13	39	30.77	1.04
26	32	30.00	1.10
33	43	27.91	0.70
Mean	38.00	29.56	0.9467
SD	5.57	1.48	0.2157
Maximum	43	30.77	1.10
Minimum	32	27.91	0.70

2. Blood lithium levels and the therapeutic range

The lithium concentrations which were required for the treatment to attain therapeutic levels were 0.5 - 1.2 mEq/L (Ward, Musa and Bailey, 1994). Most patients' lithium levels were within the desired range. Among the 42 patients included in this study, 34 patients (80.95%) had measured blood lithium levels within therapeutic range , 5 patients (11.91%) had blood lithium levels in the subtherapeutic range and 3 patients (7.14%) had blood lithium levels which were overtherapeutic range as shown in table XII. Majority of the patients had their lithium concentrations within 0.51 - 1.00 mEq/L as shown in table XIII. Table XIV, XV and XVI showed dosage regimen, lithium levels and clinical responses of the patients whose blood

lithium levels were classified as subtherapeutic , within therapeutic and overtherapeutic ranges respectively.

Table XII Percentage of patients whose blood lithium concentrations were in the subtherapeutic, therapeutic or overtherapeutic ranges.

Blood lithium level (mEq/L)	Number of patients	Percentage
subtherapeutic level (< 0.5)	5	11.91
therapeutic level (0.5 - 1.2)	34	80.95
overtherapeutic level (> 1.2)	3	7.14

Table XIII Number of patients whose measured lithium level were within various ranges.

Measured lithium level (mEq/L)	Number of patients
≤ 0.50	5
0.51 - 1.00	29
1.01 - 1.50	5
1.51 - 2.00	2
2.01 - 2.50	1
> 2.50	-

Table XIV Dosage regimen, blood lithium level and clinical response of patients whose lithium level were classified as subtherapeutic.

Patient Number	Dose (mg/day)	Blood lithium level (mEq/L)	Efficacy	Toxicity
8	600	0.42	NO	NO
14	900	0.46	YES	NO
20	900	0.30	NO	NO
21	900	0.39	YES	NO
25	900	0.47	NO	NO

Table XV Dosage regimen, blood lithium level and clinical response of patients whose lithium levels were within therapeutic range.

Patient Number	Dose (mg/day)	Blood lithium level (mEq/L)	Efficacy	Toxicity
1	600	0.90	YES	NO
10	600	0.69	NO	NO
11	600	0.73	YES	NO
15	600	0.70	NO	NO
2	900	0.62	NO	NO
4	900	0.86	YES	NO
5	900	0.58	YES	NO
6	900	0.59	YES	NO
7	900	1.03	NO	NO
9	900	0.69	NO	NO
12	900	0.54	YES	NO
16	900	0.57	NO	NO
17	900	0.63	NO	YES
18	900	1.07	YES	NO
19	900	0.58	NO	NO
22	900	0.94	NO	NO
23	900	0.53	NO	NO
24	900	0.76	NO	YES
27	900	0.57	YES	NO
28	900	0.96	YES	NO
29	900	0.70	YES	NO
30	900	0.76	YES	NO
31	900	1.00	YES	NO
32	900	0.59	YES	NO

continued.....

Patient Number	Dose (mg/day)	Blood lithium level (mEq/L)	Efficacy	Toxicity
34	900	0.68	YES	NO
35	900	0.67	YES	NO
36	900	0.92	NO	NO
38	900	1.18	YES	NO
40	900	0.70	YES	NO
41	900	0.71	NO	NO
42	900	0.53	YES	NO
13	1200	1.04	NO	NO
26	1200	1.10	YES	NO
33	1200	0.70	NO	NO

Table XVI Dosage regimen, blood lithium level and clinical response of patients whose lithium levels were classified as overtherapeutic.

Patient Number	Dose (mg/day)	Blood lithium level (mEq/L)	Efficacy	Toxicity
3	900	1.56	YES	NO
37	900	1.75	NO	YES
39	900	2.25	NO	YES

All of the 42 patients were followed up for their clinical responses. The patients were indicated as showing improvement if the undesired symptoms of the present disease was disappeared or decrease. Twenty-two

patients showed signs of improvement while sixteen patients showed no improvement and four patients had the undesired effects from the drug. Nineteen out of 34 patients (55.88 %) whose lithium levels were within therapeutic range showed improvement while two patients (5.88 %) showed toxicity. Two out of five patients (40 %) with subtherapeutic lithium levels showed improvement and none showed toxicity. One out of three patients (33.33 %) with overtherapeutic lithium levels showed improvement while two patients (66.67 %) showed toxicity.

All of the improvement signs of patients were analyzed and the side effects were monitored. Most of them were treated with the traditional dosage regimen normally prescribed by the physician. During this study, the patients had taken the drugs for some period of time before the blood lithium levels were drawn. The side effects of lithium were observed in patients No. 17, 24, 37, and 39. The patient No.17 with measured lithium level 0.63 mEq/L had tremor. The patient No.24 with measured lithium level 0.76 mEq/L had ataxia. The patient No.37 with measured lithium level 1.75 mEq/L had imbalance movement of the body. The patient No.39 with measured lithium level 2.25 mEq/L had diarrhea and tiredness.

3. Comparison between the measured and the predicted blood lithium concentrations.

Lithium is distributed in the body as a two-compartment model. It distributed initially into the plasma compartment and other rapidly

equilibrating tissues, and then pass into a more slowly equilibrating tissue compartment where it exerts its pharmacological effects in the neurons. The way which lithium distributed in the body must be considered when interpreted the serum or plasma or whole blood level because lithium is not bound to plasma protein. In this study, whole blood were collected at the proper time for meaningful indication of the clinical effects, 12 hours after the administration of the last dose of lithium in the evening of the day before collecting the sample. Every patients must take lithium at the same dosage regimen everyday for at least seven days to get steady state concentration before the blood sample was drawn. The mean measured lithium level was 0.7957 $\pm$ 0.3688 mEq/L (mean $\pm$ SD) and the range was 0.30 - 2.25 mEq/L while the mean predicted blood lithium concentration was 0.8833 $\pm$ 0.3841 mEq/L (mean $\pm$ SD) and the range was 0.35 - 2.42 mEq/L.

Table XVII presented the comparison between the measured and predicted blood lithium level.

The predicted lithium concentrations calculated by using patient serum creatinine and some physical characteristics. When the measured and predicted were compared by the paired t-test statistical method, indicated significant difference between the mean measured and predicted concentrations at the 95% level of confidence. Figure III presented the measured and predicted concentrations of the forty-two patients.

Table XVII Measured and Predicted blood lithium concentrations of each patients.

Patient Number	Measured (mEq/L)	Predicted (mEq/L)	d
1	0.90	0.88	0.02
2	0.62	0.99	-0.37
3	1.56	1.09	0.47
4	0.86	0.61	0.25
5	0.58	0.56	0.02
6	0.59	0.58	0.01
7	1.03	1.35	-0.32
8	0.42	0.62	-0.20
9	0.69	0.77	-0.08
10	0.69	0.82	-0.13
11	0.73	0.63	0.10
12	0.54	0.57	-0.03
13	1.04	1.55	-0.51
14	0.46	0.51	-0.05
15	0.70	0.90	-0.20
16	0.57	0.48	0.09
17	0.63	0.96	-0.33
18	1.07	1.52	-0.45
19	0.58	0.51	0.07
20	0.30	0.98	-0.68
21	0.39	0.65	-0.26
22	0.94	0.61	0.33

continued.....

Patient Number	Measured (mEq/L)	Predicted (mEq/L)	d
23	0.53	0.79	-0.26
24	0.76	1.39	-0.63
25	0.47	0.77	-0.30
26	1.10	1.24	-0.14
27	0.57	0.78	-0.21
28	0.96	0.81	0.15
29	0.70	0.65	0.05
30	0.76	1.06	-0.30
31	1.00	0.93	0.07
32	0.59	0.35	0.24
33	0.70	0.90	-0.20
34	0.68	1.25	-0.57
35	0.67	0.75	-0.08
36	0.92	0.57	0.35
37	1.75	0.77	0.98
38	1.18	1.42	-0.24
39	2.25	2.42	-0.17
40	0.70	0.74	-0.04
41	0.71	0.77	-0.06
42	0.53	0.60	-0.07
Mean	0.7957	0.8833	-0.08762
SD	0.3688	0.3841	
Maximum	2.25	2.42	
Minimum	0.30	0.35	

Paired T-test

$$\text{Pooled } t = \frac{\bar{d}}{S\bar{d}}$$

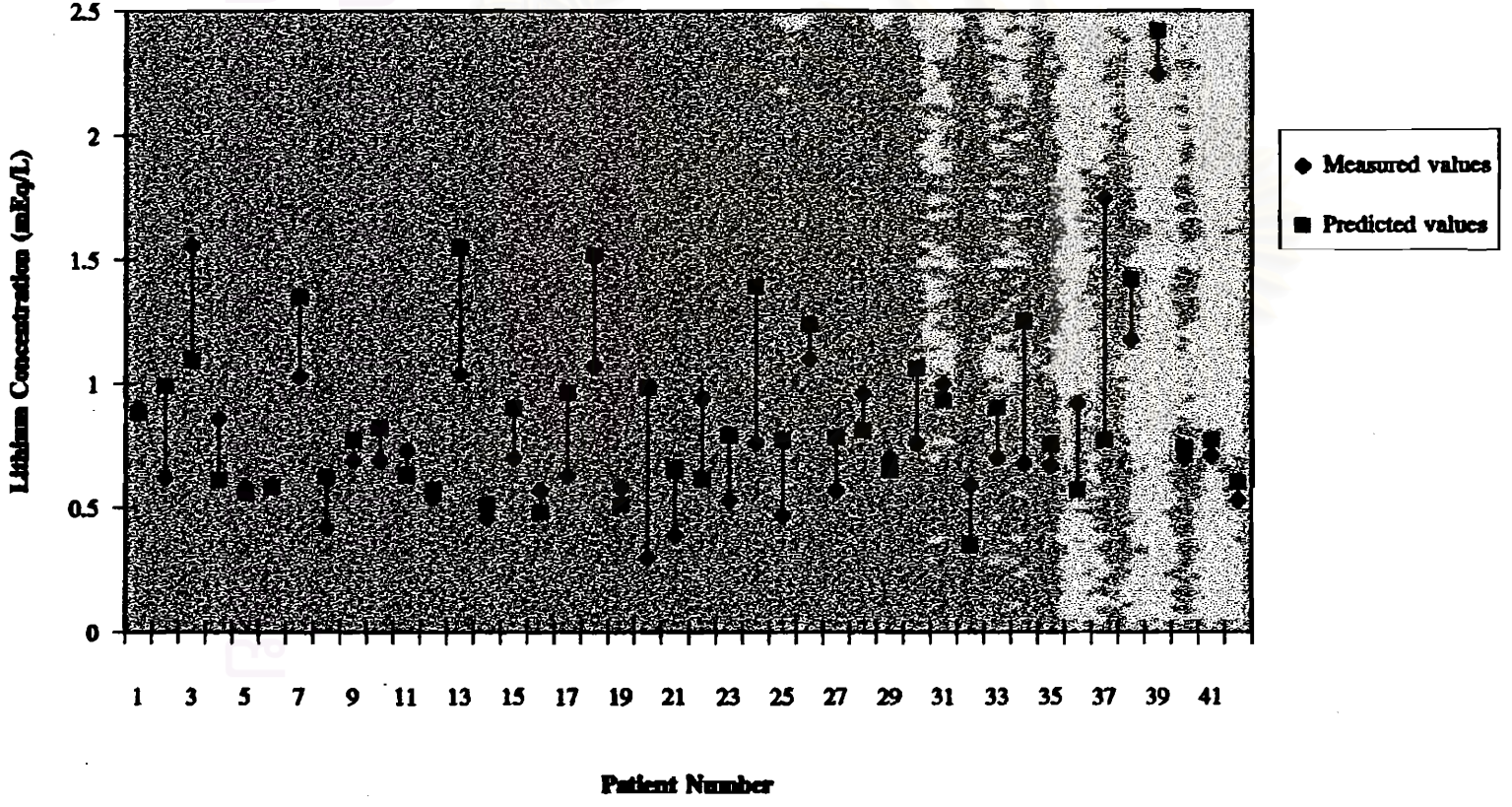
$$= \frac{-0.08762}{0.04751}$$

$$= -1.84$$

P = 0.05 , degree of freedom = 41 , t = 1.6832

P = 0.10 , degree of freedom = 41 , t = 1.3026

FIGURE III Comparison between the Measured Lithium Concentrations and the Predicted Lithium Concentrations of each patients.



4. The Adjustment of the dose using pharmacokinetic parameters

There were six patients out of the forty-two patients included in this study which dosage regimen had been adjusted to improve clinical responses.

The first patient ,patient No. 8, was diagnosed to be schizophrenia, had subtherapeutic lithium level of 0.42 mEq/L and showed no signs of improvement in her psychiatric disorder after administration of 600 mg per day of lithium carbonate for four months. She was still aggressive, agitated and anxiety. Her dosage regimen was recommended to be adjusted to 900 mg per day using pharmacokinetic theory, her psychiatric disorder were improved.

The second patient , patient No 19, was diagnosed to be mental and behavioral disorder which might cause by long term consumption of alcohol, his lithium level was 0.58 mEq/L which was within therapeutic range but showed no signs of improvement in his psychiatric disorder after treatment with 900 mg per day of lithium carbonate.. He was still anxiety, agitated and irritable mood. He also got the antidepressants, fluoxetine 20 mg ,in the morning and at noon together with antipsychotics and lithium. When the dosage regimen of lithium was adjusted to 1200 mg per day, the patient was partially improved but still had irritable mood and agitation. However, the physician continued this pattern of treatment and observe the patient's clinical response for one more week. The signs of anxiety, agitation and irritable mood had disappeared after that period of time.

The third patient, patient No.20, was diagnosed to be manic episode, had subtherapeutic lithium level of 0.31 mEq/L and showed no signs of improvement after taking lithium carbonate 900 mg per day for 15 days. He still had irritable mood and agitation. After his dosage regimen had been adjusted to be 1200 mg per day using pharmacokinetic theory, these signs were disappeared and the patient showed good clinical response.

The forth patient, patient No.25, was diagnosed to be bipolar affective disorder, had subtherapeutic lithium level of 0.47 mEq/L and showed no signs of improvement after taking lithium carbonate 900 mg per day for ten days. She still had confusion, agitation and aggression. She also had been treated with antipsychotics, haloperidol 10 mg three times a day and chlorpromazine 100 at bed time, and electroconvulsive therapy (ECT). When the dosage regimen was adjusted to be 1200 mg per day , the patient showed improvement that signs of agitation, aggression and confusion had disappeared.

The other two patients had been given lithium to control their psychiatric disorders, mood (affective) disorder, and had taken antipsychotics together with lithium carbonate. One patient, patient No.31, the lithium level was 1.00 mEq/L which was within the therapeutic range but showed signs of toxicity ,i.e., twitching, after taking lithium carbonate for 13 days, this patient also had fever which was a risk factor of causing more intoxication from lithium. After these information was informed to the physician, lithium carbonate was discontinued at once. The other patient , patient No.39, her lithium level was 2.25 mEq/L which was much higher than the therapeutic

range and she showed signs of toxicity from lithium ,i.e., diarrhea, drowsiness, after taking lithium carbonate for 9 days. Her weight was 29 kilograms. This very low weight resulted in low creatinine clearance and lithium clearance. Therefore lithium excretion rate was very slow and the patient showed lithium intoxication. The physician was informed and lithium carbonate was discontinued at once.

Table XVIII showed the details in dosage regimen and the measured blood lithium level before and after dosage adjustment in these patients.

Table XVIII Dosage regimen and the corresponding measured blood lithium levels before and after dosage adjustment in six patients.

Patient Number	Dose(1) (mg/day)	Measured(1) (mEq/L)	Dose(2) (mg/day)	Measured(2) (mEq/L)
8	600	0.42	900	0.59
19	900	0.58	1200	0.77
20	900	0.30	1200	0.66
25	900	0.47	1200	0.63
31	900	1.00	OFF	-
39	900	2.25	OFF	-

(1) = before the adjustment

(2) = after the adjustment

Although the drugs of choices of lithium are not schizophrenia ,there were many patients which were diagnosed to be schizophrenia in this study had taken lithium as adjunctive therapy if antipsychotic drugs alone could not control their psychiatric disorders.

Lithium was used in patient No.8 which was diagnosed to be schizophrenia as adjunctive therapy with antipsychotic drugs. However, her psychiatric disorders were not improved after added lithium for four months. Her blood lithium level was too low to control her psychiatric disorders. Therefore her lithium dosage adjustment was needed.

The patient No.19 had taken lithium carbonate to control the positive symptoms of his psychiatric disorders. He was diagnosed to be mental and behavior disorders due to alcohol. Although his blood lithium level was within therapeutic range , his psychiatric symptoms were not fully cured. Therefore dosage adjustment was needed in this case.

Lithium was used to control bipolar affective disorder in patient No.20 and patient No.25. The blood lithium level before adjusting the dosage regimen in these patients was too low to control psychiatric disorders, therefore the adjustment of dosage regimen was needed.

The blood lithium level obtained from the patient No.31 and patient No.39 were evaluated along with their clinical responses which indicated intoxication of lithium. Although the blood lithium level obtained from the patient No.31 was within therapeutic range, she had showed signs of intoxication. The blood lithium level obtained from patient No.39 was overtherapeutic level and she showed sign of toxicity concurrently. Her

creatinine clearance was 27.77 ml/min. and her lithium clearance was 7.5 ml/min. which was very low. This could be the cause of lithium intoxication because lithium was excreted from the body very slowly. However, when the weight of the patient was taken into consideration, it showed that the patient was very thin, she weighs only 29 kilograms. Her dosage calculated as milligram per kilogram per day was 31.03 which was very high and should be the cause of intoxication. The physician was informed about blood lithium level and signs of toxicity then she discontinued lithium carbonate at once. The dosage adjustment was needed in these two cases to get lower blood lithium level but the physician wanted to make sure about patient's safety, so she discontinued lithium carbonate in stead of reducing the dosage of lithium carbonate.

5. Prediction of Creatinine Clearance from Serum Creatinine.

The serum creatinine of forty-two patients were obtained from the patient' data charts. Table XIX showed the ranges of serum creatinine, the ranges of creatinine clearance calculated from equation 1-2 in appendix A and the number and percentage of patients with various ranges of serum creatinine and creatinine clearances.

Table XIX The range of serum creatinine and creatinine clearance along , with the number of patients and the percentage.

Serum creatinine (mg/dL)	Creatinine clearance (ml/min.)	Number of patients (percent)
< 0.5	-	-
0.5 - 1.0	< 50.00	3 (7.14)
	50.01 - 70.00	9 (21.43)
	70.01 - 90.00	10 (23.81)
	90.01 - 110.00	4 (9.52)
	110.01 - 130.00	7 (16.67)
	> 130.00	4 (9.52)
> 1.0	< 50.00	1 (2.38)
	50.01 - 70.00	1 (2.38)
	70.01 - 90.00	3 (7.14)
	90.01 - 110.00	-
	110.01 - 130.00	-
	> 130.00	-

6. Lithium Clearances versus Creatinine Clearances

In this study, the mean serum creatinine, creatinine clearance were 0.8428 ± 0.1876 mg per dL and 86.0229 ± 32.3356 ml per min. respectively. The estimation of lithium clearance as approximately 25 percent of creatinine clearance according to equation 3 in Appendix A along with the lithium clearance calculated from lithium blood levels were shown in table XX.

7. Lithium Clearances calculated from Creatinine Clearances and Lithium Clearances calculated from Measured Blood Lithium Levels.

Using paired t-test to compare values of lithium clearances calculated from creatinine clearances and from measured blood lithium levels showed significant difference between these two mean values at the 95 % level of confidence indicated that lithium clearances obtained from different methods in this study could not be used substantially. Table XX and figure IV showed comparison between lithium clearances calculated from serum creatinine and those from measured blood lithium levels.

From this study, the serum creatinine of the patients who showed lithium adverse effects were 0.7 (patient No.17), 1.3 (patient No.24), 1.1 (patient No.37), 0.9 (patient No.39), and 0.8 (patient No.41) mg per dL

which were all in the normal range . The relationship between lithium toxicity and the patients' serum creatinine could not be observed from this study , much greater number of patients should be studied before any conclusion could be made.

Table XX Serum creatinine , creatinine clearance , Lithium clearance calculated from serum creatinine and Lithium clearance calculated from measured blood lithium level of each patients.

Patient Number	Scr (mg/dL)	Clcr (ml/min.)	ClLi(1) (ml/min.)	ClLi(2) (ml/min.)	d
1	1.0	51.3069	12.8267	12.5300	0.2967
2	0.9	68.0555	17.0139	27.2850	-10.2711
3	0.7	62.1563	15.5391	10.8433	4.6958
4	0.7	110.2976	27.5744	19.6700	7.9044
5	1.0	121.3333	30.3333	29.1667	1.1666
6	0.6	116.8750	29.2187	28.6717	0.5470
7	0.9	50.1343	12.5336	16.4233	-3.8897
8	0.6	72.5255	18.1314	26.8517	-8.7203
9	1.1	88.6364	22.1591	24.5167	-2.3576
10	0.9	54.6335	13.6584	16.3450	-2.6866
11	0.8	71.8958	17.9739	15.4483	2.5256
12	0.7	118.3928	29.5982	31.3267	-1.7285
13	0.8	58.1276	14.5319	21.6883	-7.1564
14	0.6	131.7303	32.9326	36.7750	-3.8424
15	0.9	50.1342	12.5335	16.1283	-3.5943
16	0.8	141.3194	35.3297	29.6783	5.6514
17	0.7	71.0357	17.7589	26.8517	-9.0928
18	0.9	44.3889	11.0972	15.8100	-4.7128

continued.....

Patient Number	Scr (mg/dL)	Clcr (ml/min.)	ClLi(1) (ml/min.)	ClLi(2) (ml/min.)	d
19	0.7	133.1349	33.2837	29.1667	4.1170
20	1.0	68.8750	17.2187	34.1750	-16.9563
21	0.8	103.3333	25.8333	43.3767	-17.5734
22	0.8	110.4167	27.6042	17.9967	9.6076
23	1.2	85.4629	21.3657	31.9183	-10.5526
24	1.3	48.8942	12.2235	23.1733	-10.9488
25	0.9	87.2299	21.8075	35.9933	-14.1858
26	0.7	72.8571	18.2143	20.5050	-2.2907
27	0.8	86.0625	21.5156	29.6783	-8.1627
28	1.0	83.7083	20.9271	17.6217	3.3054
29	0.9	102.6821	25.6705	24.1667	1.5038
30	1.0	64.0000	16.0000	22.2583	-6.2583
31	0.8	72.5156	18.1289	16.9167	1.2122
32	0.5	192.1000	48.0250	28.6717	19.3533
33	0.7	100.0794	25.0198	32.2217	-7.2019
34	1.3	53.8461	13.4615	24.8767	-11.4152
35	0.8	89.8698	22.4674	25.2483	-2.7809
36	0.9	118.5802	29.6451	18.3883	11.2568
37	1.1	87.9798	21.9949	9.6667	12.3282
38	0.7	47.8631	11.9658	14.3367	-2.3709
39	0.9	27.7693	6.9423	7.5183	-0.5760

continued.....

Patient Number	Scr (mg/dL)	Clcr (ml/min)	ClLi(1) (ml/min)	ClLi(2) (ml/min)	d
40	0.7	91.8303	22.9576	24.1667	-1.2091
41	0.8	87.6563	21.9141	23.8267	-1.9126
42	0.5	113.2389	28.3097	31.9167	-3.6070
Mean	0.8428	86.0229	21.3342	23.6618	-2.1560
SD	0.1876	32.3356	8.0743	7.9799	
Maximum	1.3	192.1000	48.0250	43.3767	
Minimum	0.5	27.7693	6.9423	7.5183	

(1) = calculated from serum creatinine

(2) = calculated from measured blood lithium level

Paired T-test

$$\text{Pooled } t = \frac{\bar{d}}{S_{\bar{d}}}$$

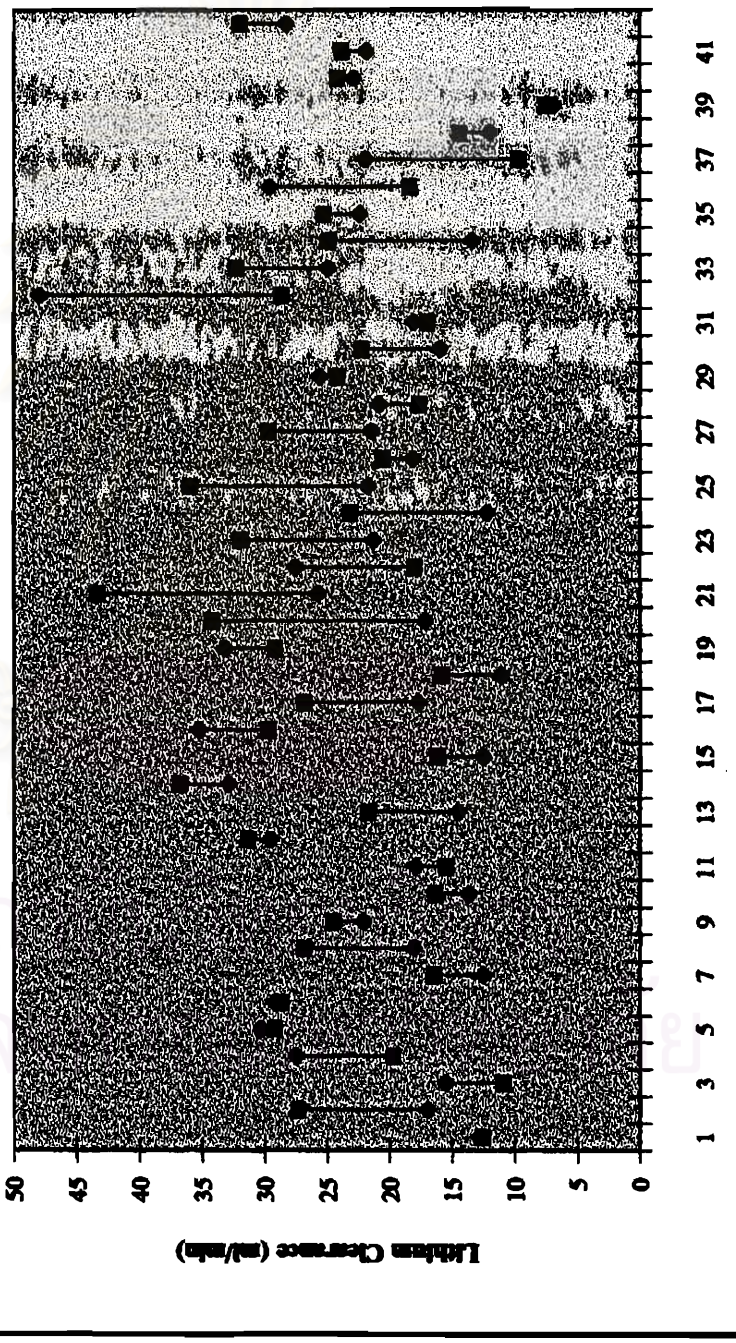
$$= \frac{-2.156}{1.194}$$

$$= -1.81$$

P = 0.05 , degree of freedom = 41 , t = 1.6832

P = 0.10 , degree of freedom = 41 , t = 1.3026

FIGURE IV Comparison between Lithium Clearances calculated from Serum Creatinine and from Measured Lithium Concentrations of each patients.



8. The Accuracy of the Prediction of Blood Lithium Levels calculated from serum creatinine and those calculated from lithium clearances.

In patient No 8. ,there was little difference between measured blood lithium level and blood lithium level predicted from lithium clearance calculated from measured blood lithium level while there were some difference between measured blood lithium level and blood lithium level predicted from serum creatinine.

In patient No. 19, 20, and 25 there was no difference between measured blood lithium level and blood lithium level predicted from lithium clearance calculated from measured blood lithium level while there were some difference between measured blood lithium level and blood lithium level predicted from serum creatinine.

These indicated that blood lithium levels predicted from lithium clearances were more accurate than those predicted from serum creatinine. Therefore dosage adjustment shold be calculated from pharmacokinetic parameters derived from measured blood lithium levels in stead of those calculated from patients' serum creatinine. However , we can use serum creatinine and other general datas of the patients for approximate dosage adjustment calculation in clinical practice.

Table XXI showed the difference between the measured blood lithium levels and predicted blood lithium levels calculated from serum creatinine and those calculated from lithium clearances.

Table XXI The difference between the measured blood lithium levels and the blood lithium levels predicted from serum creatinine and those predicted from lithium clearances.

Patient Number	Measured Level (mEq/L)	Predicted Level (1) (mEq/L)	Predicted Level (2) (mEq/L)	d(1)	d(2)
8	0.59	0.93	0.63	0.34	0.04
19	0.77	0.68	0.77	-0.09	0.00
20	0.66	1.31	0.66	0.65	0.00
25	0.63	1.03	0.63	0.40	0.00

(1) = predicted from serum creatinine

(2) = predicted from lithium clearance

d(1) = Difference between measured level and predicted level (1)

d(2) = Difference between measured level and predicted level (2)

Besides the forty-two patients included in this study , there were two patients who were admitted and had taken lithium to control their illness but their data and results were not included since their lithium dosing interval was once daily which was not matched to the criteria of the standard 12 hours after last dose blood lithium level determination.

One patient was a woman aged 18, weigh 48 kilograms, she was diagnosed to be unspecified mental retardation. Her lithium dosage regimen was 300 mg once daily. Her blood lithium level 24 hours after last dose at trough level was 0.26 mEq/L. She had taken antipsychotics together with lithium. After she had taken lithium for 2 weeks, she showed signs of improvement but not cured. Her serum creatinine , creatinine clearance and lithium clearance were 0.7 mg per dL, 98.76 ml per min. and 24.69 ml per min. respectively.

The other patient was a woman aged 67 , weigh 50 kilograms, she was diagnosed to be schizophrenia. Her lithium dosage regimen was 300 mg once daily. Her blood lithium level 24 hours after last dose at trough level was 0.24 mEq/L. She had taken antipsychotic drug as well. She developed signs of toxicity after taking lithium for 10 days. She had severe nausea so the physician discontinued all psychotropic drugs. One day later, she felt better and had no nausea or vomiting. Two days later, the physician tried psychotropic drugs and lithium again. At this time no , signs of intoxication had occurred. Her serum creatinine, creatinine clearance and lithium clearance were 1.0 mg per dL, 43.0903 ml per min., and 10.77 ml per min. respectively.