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Effects of Long-Term Lithium Treatment on Kidney Function

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ABSTRACT. This study was carried out to examine the renal function of patients receiving treatment with Li_2CO_3. Blood and urine samples were collected to measure plasma AMG, plasma BMG, urinary ALB, urinary AMG, urinary BMG and urinary NAG.

A significant correlation was found between the age at the beginning of treatment and the present age and the degree of glomerular damage. No significant correlation was found between the degree of glomerular damage and either the length of treatment or the total dose of Li_2CO_3. A significant correlation was found between glomerular damage and the daily dose of Li_2CO_3 or the plasma lithium concentration. A significant correlation was also noted between proximal tubular damage and the daily dose of Li_2CO_3 or the plasma lithium concentration.

It was concluded that in patients receiving with lithium age is a risk factor for glomerular damage but not for proximal tubular damage, that long-term administration is not a risk factor for glomerular or proximal tubular damage and that an increase in the dose of Li_2CO_3 or in the plasma lithium concentration represents a risk factor for glomerular damage and proximal tubular damage.

Key words : lithium — kidney function — α_1-microglobulin — β_2-microglobulin

Despite the frequent long-term use of Li_2CO_3, scarcely any systematic studies regarding the renal function of patients under such treatment have been reported.

Increases in the concentrations of α_1-microglobulin (AMG) and β_2-microglobulin (BMG) in plasma reflect glomerular damage, and their increased concentrations in urine are indicative of proximal tubular dysfunction. Increased concentration of N-acetyl-β-D-glucosaminidase (NAG) in urine also reflects proximal tubular damage.

In the present study, therefore, measurement of these substances was carried out in patients taking Li_2CO_3, along with a survey of their age at the beginning of treatment, their present age, length of treatment, total dose of Li_2CO_3, daily dose of Li_2CO_3 and plasma lithium concentration.

The correlation between the former and latter sets of data was then evaluated.

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MATERIALS

This study was conducted on 40 outpatients, 21 males and 19 females, receiving treatment with Li_2CO_3 at the Department of Psychiatry, Kawasaki Medical School Hospital between January 20 and March 31, 1989. Informed consent for participation in this clinical trial was obtained from all patients prior to the beginning of the trial.

Based on ICD-9, manic-depressive psychosis of the circular type was found in 31 patients, manic-depressive psychosis of the depressed type in 4, schizophrenic psychosis of the schizoaffective type in 4 and Gilles de la Tourette syndrome in 1.

METHODS

Blood and urine samples were collected at 6 a.m. for the measurement of plasma AMG, plasma BMG, urinary ALB, urinary AMG, urinary BMG and urinary NAG.

The age at the beginning of treatment, present age, length of treatment, total dose of Li_2CO_3, daily dose of Li_2CO_3 and the plasma lithium concentration were also studied.

Correlation between the first and second sets of data was then evaluated.

RESULTS AND DISCUSSION

The age at the beginning of treatment (Age-B) ranged from 13 to 67 years, with a mean age of 43.75 ± 14.39. The age at present (Age-P) ranged from 13 to 76 years, with a mean age of 47.83 ± 15.25. The length of treatment (LT) ranged from 1 to 182 months, with a mean length of 47.04 ± 43.15 months. The total dose of Li_2CO_3 (TD) was $18 \sim 2988$ g, with the average dose being 795.25 ± 735.35 g. The daily dose of Li_2CO_3 (DD) was $200 \sim 1200$ mg, with the average dose being 647.50 ± 264.08 mg. The plasma lithium concentration (PLC) was $0.07 \sim 0.98$ mEq/l, with an average of 0.442 ± 0.215 mEq/l.

Table 1 summarizes the mean values of plasma AMG, plasma BMG, urinary ALB, urinary AMG, urinary BMG and urinary NAG. Table 2 shows the correlation coefficients between the first and second sets of data.

As shown in Table 2, there was a significant correlation between Age-B and Age-P and the degree of glomerular damage. These results correspond with reports that a significant correlation was found between age and the

TABLE 1. Mean values of the data

plasma AMG	19.30 ± 4.71	(mg/l)
plasma BMG	1.46 ± 0.61	(μg/ml)
urinary ALB	18.48 ± 24.20	(μg/ml)
urinary AMG	5.17 ± 7.06	(mg/l)
urinary BMG	370.6 ± 1131.6	(μg/l)
urinary NAG	4.24 ± 3.17	(U/l)
urinary AAP	21.40 ± 12.86	(U/l)

TABLE 2. Correlation coefficients between the first and second sets of data

		Age-B	Age-P	LT	TD	DD	PLC
plasma	AMG	c0.318	0.311	0.044	0.132	0.042	0.188
plasma	BMG	a0.545	a0.573	0.168	0.216	−0.005	c0.385
urinary	ALB	0.044	0.047	0.023	0.272	b0.423	0.271
urinary	AMG	0.192	0.198	0.003	0.091	c0.372	a0.542
urinary	BMG	0.181	0.162	−0.108	−0.002	c0.333	b0.471
urinary	NAG	0.199	0.202	0.023	0.114	0.127	b0.466

a : $p < 0.001$, b : $p < 0.01$, c : $p < 0.05$

Age-B = age at the beginning of treatment; Age-P = age at present; LT = length of treatment; TD = total dose of Li_2CO_3; DD = daily dose of Li_2CO_3; PLC = plasma lithium concentration

glomerular filtration rate.[1,2] A scattergram of Age-P and plasma BMG is shown in Fig. 1. Results indicated that attention should be paid to glomerular damage in patients who are more than 50 years old.

No significant correlation was found between glomerular damage and either LT or TD. These results correspond with reports that no significant correlations have been found between creatinine clearance and LT[3]. They also indicate that no problems are therefore expected with the long-term use of Li_2CO_3.

A significant correlation was found between the glomerular damage and DD or PLC. These results correspond with reports that significant correlation was found between creatinine clearance and DD or PLC.[3] A scattergram of DD and urinary ALB is shown in Fig. 2, and one of PLC and plasma BMG in Fig. 3. These results indicate that attention should be paid to glomerular damage when DD is higher than 600 mg or PLC exceeds 0.3 mEq/1.

A significant correlation was also noted between proximal tubular damage and DD or PLC. A scattergram of DD and urinary BMG is shown in Fig. 4, and one of PLC and urinary AMG in Fig. 5. Lavender et al.[4] reported a
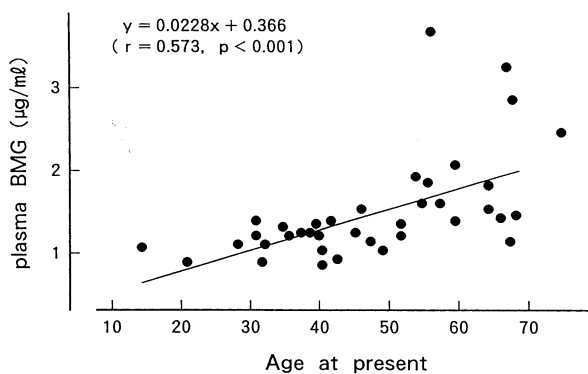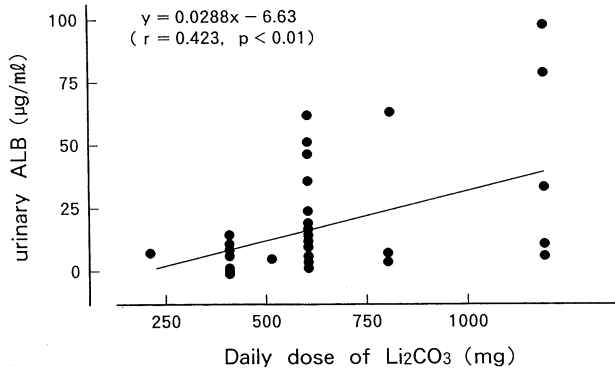

Fig. 1. Scattergram of Age-P and plasma BMG

$y = 0.0288x - 6.63$
$(r = 0.423, \quad p < 0.01)$

Fig. 2.   Scattergram of DD and urinary ALB

$y = 1.09x + 0.977$
$(r = 0.385, \quad p < 0.05)$
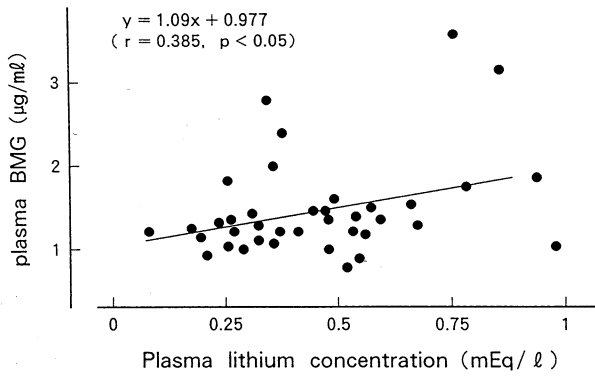
Fig. 3.   Scattergram of PLC and plasma BMG

$y = 1.43x - 554$
$(r = 0.333, \quad p < 0.05)$
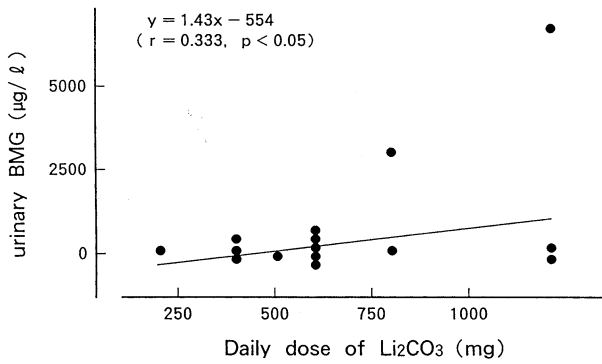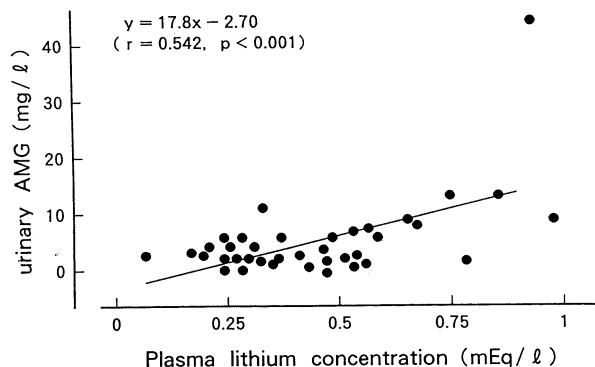
Fig. 4.   Scattergram of DD and urinary BMG

Fig. 5. Scattergram of PLC and urinary AMG

case of deceased patient with a PLC of 5.2 mEq/l and organic proximal tubular damage. Our results indicate that attention should be paid to proximal tubular damage when DD is higher than 500 mg or PLC exceeds 0.75 mEq/l.

SUMMARY

The following conclusions were drawn regarding patients receiving treatment with Li_2CO_3.
1. Age is a risk factor for glomerular damage, but not for proximal tubular damage.
2. Long-term administration is not a risk factor for either glomerular or proximal tubular damage.
3. An increase in the dose of Li_2CO_3 or an increase in the lithium concentration in plasma represents a risk factor for both glomerular damage and proximal tubular damage.

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