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EFFECTS OF LONG-TERM LITHIUM CARBONATE TREATMENT ON THYROID FUNCTION IN PSYCHIATRIC PATIENTS

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SUMMARY

The effect of long-term lithium carbonate treatment on thyroid function was investigated in 40 clinically euthyroid patients with Manic Depressive Psychosis. Before lithium treatment, all patients showed normal levels (T_4) of serum total thyroxine, free thyroxine index and thyrotropin (TSH). After lithium carbonate treatment for a mean period of 24 months, these patients did not show any significant change in the mean values of serum total T_4, free thyroxine index and TSH. None showed clinical symptoms of goitre and hypothyroidism after long-term lithium treatment. It is concluded that lithium therapy in euthyroid psychiatric patients has no adverse effect on thyroid function and on the pituitary secretion of TSH.

Lithium salts have been increasingly used in the treatment of patients with psychiatric illnesses. The toxic effects of lithium have been well documented and, of the various endocrine and metabolic effects reported to date, thyroid dysfunction has received the most widespread attention. Lithium carbonate treatment in psychiatric patients was found to induce a fall in serum total thyroxine (T_4), (Emerson *et al.*, 1973) and an elevation in serum thyrotropin (TSH) (Lazarus and Bennie, 1972; Emerson *et al.*, 1973). In addition, the development of goitre (Schou *et al.*, 1968) and clinically evident hypothyroidism (Luby *et al.*, 1971; Rogers and Wybrow 1971; Candy, 1972) have been occasionally observed during lithium therapy. On the other hand, we have noticed that lithium treatment in clinically euthyroid psychiatric patients did not show any significant alteration in thyroid function. The details are reported in this communication.

MATERIALS & METHODS

40 psychiatric patients (30 males and 10 females) between the ages of 20 and 60 years were the subjects of the study. They attended the psychiatry unit of Christian Medical College Hospital for treatment of recurrent episodes of Manic Depressive Psychosis. Those who gave a history of having had 3 or more major episodes of mania and/or depression in the previous 2 years were taken up for prophylactic treatment with lithium carbonate. 26 of them had both recurrent manic and depressive episodes, 10 had only recurrent manic episodes, while 4 gave only a hisotry of recurrent depression.

Those who came in a state of depression (18 in number) were treated for the current episode, with tricyclic antidepressants and after the depressed mood improved, they were started on lithium as a prophylactic. 22 patients who came in a state of mania or hypomania were initially treated with phenothiazines for the control of manic symptoms and within a few days they were also given lithium both for the control of the current manic episode as well as for prevention of future episodes. Once lithium reached an effective level, the phenothiazines were gradually tapered off and later was used only for brief periods in 5 of these patients in

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whom recurrence occurred despite lithium treatment. Only those who had been on long term lithium treatment for at least two years were studied.

All subjects were medically evaluated and showed no evidence of significant liver, cardiac or renal disease. They were without goitre and had no sign of thyroid disorders. Subsequent medical examination and investigations indicated that all of them were euthyroid as well.

The dosage of lithium was 600 to 1800 mg., daily, and serum lithium concentration was 0.83±0.20 mEq/l. Blood samples were collected before and after lithium treatment for thyroid function studies. Serum T_4 and TSH were measured by specific and sensitive radio immunoassays and the methodological details were described in an earlier report from our laboratory (Neela *et al.*, 1981). Using Sephadex T_3 uptake test, free thyroxine index was calculated. Fifty healthy control subjects studied by us earlier (Neela *et al.*, 1981) were used for comparison.

TABLE 1. *Effect of Lithium on Thyroid function tests in psychiatric patients*

Group	T_4 (nmol/l)	Free Thyroxine index	TSH (nU/ml)
Psychiatric patients (N=40)			
Before lithium	114±19	116±19	4.2±2.1
After lithium	111±23	112±25	4.3±1.6
*Control subjects (N=50)	113±24	117±24	4.4±1.8

Each value represents the Mean± Standard dexiation

Comparison between the values before and after lithium treatment was made, and no significant difference was established.

*Referred from our previous report (Neela et al., 1981).

As shown in the table, before starting the lithium treatment, all euthyroid psychiatric patients had serum total T_4, free thyroxine index and TSH comparable to that seen in control subjects. After lithium therapy none of our psychiatric patients showed an elevation of serum TSH level above the reference range (0.8—8.0 uU/ml) of control subjects. Serum T_4 level also did not fall below the reference range of control group (65—161 nmol/l). The mean values of serum T_4, free thyroxine index, and TSH did not alter significantly after lithium treatment, compared to baseline levels. None of our patients had symptoms of clinical hypothyroidism or goitre during the course of lithium treatment.

DISCUSSION

A major finding in the present study is that there was no evidence of clinical or biochemical hypothyroidism after lithium therapy. It has been reported earlier (Emerson *et al.*, 1972) that the mean serum TSH in the lithium treated group was three times higher than in the control group, and elevated TSH levels occurred in 30% of the patients at some time during treatment. Also, Lazarus and Bennie (1972), noticed that there was a rise in plasma TSH level in 13 manic-depressive patients on lithium for three months and another 12 patients who had been on lithium for 20 months exhibited still higher TSH levels than the values of the former group. In the present study, the mean serum TSH value after lithium treatment did not alter significantly when compared with pretreatment level or with healthy control subjects. None of our patients showed an increase in serum TSH level above the reference range of control subjects during lithium therapy. The patients on lithium treatment in our study were reassessed for thyroid function after long-term lithium carbonate treatment (Minimum period

24 months). But none showed any signs of clinical or biochemical hypothyroidism.

Regarding the possible effect of lithium on circulating thyroid hormones, Rifkin *et al.* (1974), while comparing the 6 weeks lithium treatment period with placebo period in psychiatric patients noticed a significant drop in the mean serum T_4 level after lithium intake. Cooper and Simpson (1969) also found that the mean PBI and free T_4 levels were significantly reduced in 25 manic-depressives when compared with 139 other psychiatric admissions. On the other hand, it has been reported (Emerson *et al*, 1973; Burrow *et al.*, 1971) that after about one to eight months lithium treatment, there was a noticeable but statistically insignificant fall in serum T_4 concentration in manic-depressive patients. The present study in agreement with these authors, shows a slight but not significant fall in serum T_4 and free thyroxine index when compared with pre-treatment level and with control subjects.

The mechanism of action of lithium on thyroid gland remains unclear. Lithium alone was found to decrease the I^{131} release by 30 to 85% in thyrotoxic patients treated with lithium carbonate (Temple *et al.*, 1972). Evidence that lithium accumulate within the thyroid gland generally achieving a level of 3 to 5 times that in the serum and that lithium inhibits the release of iodine from thyroid was also demonstrated (Burrow *et al.*, 1971). A slight reduction of serum T_4 and free thyroxine index noticed by us might reflect such influences of lithium on the thyroid gland. The evidence is indirect and must stand as a tentative hypothesis. However, our findings support the conclusion that lithium therapy has no adverse effect on thyroid function and on the pituitary secretion of TSH in clinically euthyroid psychiatric patients.

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